



Preoperative optimization in total joint arthroplasty

Infection risk and health effect

Cooperation of hospital and primary health care

María Sigurðardóttir

Thesis for the degree of Philosophiae Doctor

September 2025

School of Health Sciences

FACULTY OF MEDICINE

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Samvinna Sjúkrahúss og Heilsugæslu

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Ágrip

Áhrif heilsuefningar á mótanlega áhættuþætti fyrir fyrstu liðskiptaaðgerð á tíðni skurðsýkinga og almenna heilsu. Samvinna Sjúkrahúss og Heilsugæslu

Inngangur

Liðskiptaaðgerðir á neðri útlimum eru meðal árangursríkustu meðferðarúrreða sem innleiddar hafa verið á seinustu áratugum. Þær draga úr verkjum og bæta verulega lífsgæði sjúklinga með endastígs slitgigt og langflestir sjúklingar fá góðan og viðvarandi bata. Sýkingar í kjölfar liðskipta geta þó haft alvarlegar afleiðingar og valdið þörf á endurteknum aðgerðum, langtíma sýklalyfjameðferð, aukið á almenn veikindi og dánartíðni og eru verulega kostnaðarsamar fyrir sjúklinginn og samfélagið.

Til að draga úr áhættu á fylgikvillum hefur áhugi aukist seinustu ár á heilsuefningu mótanlegra áhættuþátta fyrir aðgerð sem þekkt er að tengjast liðsýkingum. Þar má nefna ofþyngd, sykursýki, blóðskort, vannæringu, reykingar og þrekleysi.

Slík heilsuefandi ferli hafa verið skipulögð með mismunandi hætti og einnig er breytileiki í fjölda áhættuþátta sem reynt er að hafa áhrif á. Lítið hefur verið birt af rannsóknum um árangur þeirra og flestar þeirra eru aftursæjar.

Markmiðið með þessu verkefni var að innleiða heilsuefandi ferli til að bæta mótanlega áhættuþætti í bið eftir liðskiptaaðgerð, í þeim tilgangi að fækka sýkingum og fylgikvillum eftir aðgerð og kanna hvort í kjölfarið yrðu einnig áhrif á almenna heilsu.

Aðferðir

Gerð var framsæ tilfella viðmiða rannsókn (e. *prospective case control study*) á áhrif fjölþátta heilsuefandi ferils sem skipulagður var í samvinnu sjúkrahúss og heilsugæslu.

Sjúklingarnir í viðmiðunarhóp voru þegar á biðlista eftir liðskiptaaðgerð þegar rannsóknin hófst. Þeir höfðu fengið hefðbundinn undirbúning fyrir aðgerðina og voru teknir inn í rannsóknina við heimsókn á miðstöð undirbúnings fyrir aðgerð einni viku fyrir aðgerð.

Sjúklingarnir í rannsóknarhóp voru teknir inn í rannsóknina á göngudeild bæklunar við heimsókn þangað eftir tilvísun frá heimilislækni 6-12 mánuðum fyrir aðgerð. Blóðprufur voru teknar og líkamsmassastuðull mældur, (e. *Body Mass Index, BMI*) og þeim vísað til heimilislæknis innan 2-3 vikna til mats á niðurstöðum og hvort frekari meðferð eða ráðgjafar væri þörf. Sjúklingum sem voru með líkamsmassastuðul ≥ 40 fengu ráðgjöf frá næringarfræðingi og þeir sem voru með D-vítamín gildi < 50 nmol/L var ráðlagt að taka uppþót. Vannæring var einnig metin.

Hjá báðum hópum, einni viku fyrir aðgerð, voru teknar blóðprufur og líkamsmassastuðull mældur og þeir svöruðu spurningakönnun um undirbúningstímabilið fyrir aðgerðina. Báðum hópum var svo fylgt eftir á sama hátt eftir aðgerð.

Gögnum var safnað um lýðfræðilega þætti, aðgerð, undirliggjandi sjúkdóma (ASA flokkun), blóðprufur, blóðgjafir, lengd sjúkrahússdvalar, fylgikvilla eftir aðgerð og dánartíðni. Skráðar voru grunnar skurðsárasýkingar og dýpri liðsýkingar ásamt frekari fylgikvillum og enduraðgerðir. Eftir aðgerðina voru einnig skráðar langtíma og bráðar sjúkdómsgreiningar og andlát. Upplýsingar um komur á bráðamóttöku, innlagnir á sjúkrahús og gjörgæslu voru og fengnar.

Niðurstöður

Í rannsókninni voru í viðmiðunarhóp 738 sjúklingar af 744 sem samþykktu þátttöku, og gengust undir aðgerð frá ágúst 2018 til september 2020. Í rannsóknarhóp voru 746 sjúklingar af 1010 sem samþykktu þátttöku en 259 sjúklingar höfnuðu þegar þeim var boðin aðgerð. Þeir biðu að miðgildi í 307 daga eftir aðgerð sem voru framkvæmdar frá mars 2019 til desember 2022. Í viðmiðunarhóp urðu 5% aðgerðanna á meðan Covid-19 faraldrinum stóð en 77% í rannsóknarhóp.

Í viðmiðunarhópnum fannst samband milli ofþyngdar ($BMI \geq 30$) og sykursýki/röskunar á sykurstjórnun ($HbA1c \geq 42$ mmol/mol) og tilurð grunnra skurðsárasýkinga sem bentu til þess að með því að bæta mótanlega áhættuþætti fyrir aðgerð mætti hugsanlega draga úr fylgikvillum.

Heilsuefandi ferlið hjá rannsóknarhópnum tengdist marktækt meiri vitund um áhættuþætti og vilja fyrir lífsstílsbreytingum og bætingu á þyngd, blóðþurrð, sykursýki og vítamín D gildum í bið eftir aðgerð.

Einni viku fyrir aðgerð voru hóparnir þannig sambærilegir, nema að mun hærra hlutfall var af undirliggjandi sjúkdómum/sjúkdómsbyrði í rannsóknarhópnum (ASA flokkun 3-4 32% á móti 23%).

Við sex vikur eftir aðgerð þegar leiðrétt var fyrir mun í ASA-flokkun (sem endurspeglar undirliggjandi sjúkdóma), aldri og kyni þá voru sjúklingar í

rannsóknarhópnum í minni hættu á að greinast með grunnna skurðsýkingu samanborið við viðmiðunarhópinn (OR 0,64; 95%CI 0,42 – 0,97). Einnig voru marktækt færri fylgikvillar frá Aðgerðasvæðinu eða 11.3% á móti 15.7% (Munur – 4.5%; 95%CI –8.0 to –1.0).

Einu ári eftir aðgerð var tíðni grunnra skurðsýkinga 5.9% í rannsóknarhóp á móti 7.9% í viðmiðunarhóp en ekki marktækur munur á milli þeirra (HR 0.67; 95%CI 0.45–1.01). Ekkert samband fannst milli áhættuþátta og tíðni grunnra skurðsýkinga í rannsóknarhópnum en var til staðar í viðmiðunarhópnum við BMI ≥ 30 og HbA1c ≥ 42 mmol/mol.

Þrem árum eftir aðgerð var tíðni djúpra liðsýkinga 2.0% í rannsóknarhóp á móti 1.1% í viðmiðunarhóp (HR 1.80; 95% CI 0.76–4.30). Djúpar liðsýkingar áttu uppruna sinn í grunnnum skurðsárasýkingum í 80% tilfella í rannsóknarhóp og 88% í viðmiðunarhóp og sambærilega 95% og 98% þeirra áttu sér stað innan sex vikna.

Þróun frá grunnnum skurðsárasýkingum í djúpar liðsýkingar var algengari í rannsóknarhópnum (27.3%) en í viðmiðunarhópnum (12.1%).

Þremur árum eftir aðgerð fannst ekki munur á almennu heilsufari né dánartíðni á milli hópanna.

Ályktanir

Tiltölulega einfalt og skýrt heilsueflandi ferli fyrir aðgerð jók vilja sjúklinga til lífsstílsbreytinga og bætti mótanlega áhættuþætti fyrir aðgerð og minnkaði skammtíma tíðni grunnra skurðsárasýkinga og fylgikvilla frá skurðsvæði. Hins vegar hafði inngripíð ekki marktæk langtíma áhrif á tíðni grunnra skurðsárasýkinga, djúpra liðsýkinga, almenns heilsufars né dánartíðni. Truflandi þættir, aðallega Covid-19 faraldurinn og flutningur liðskiptaaðgerða til annarra stofnana á rannsóknartímabilinu gætu hafa haft áhrif á niðurstöður. Niðurstöðurnar benda á mikilvægi þess að gera framsæjar rannsóknir á árangri heilsueflandi ferla og jafnframt að meta áhrif utanaðkomandi þátta á meðferðarárangur. Frekari rannsóknir innan sviðsins er því þörf.

Leitarorð:

Heilsuefling fyrir aðgerð, liðskiptaaðgerð, áhættuþættir, skurðsárasýking, liðsýking

Abstract

Effect of preoperative optimization on surgical infections and general health in primary total joint arthroplasty. Cooperation of Hospital and Primary Health Care

Introduction

Lower extremity total joint arthroplasty (TJA) reduces pain and improves quality of life in individuals with end-stage osteoarthritis, with the majority of cases achieving long-lasting, favorable outcomes. However, infectious complications at the surgical site can be devastating and costly for both patients and society, requiring repeated surgeries and prolonged antibiotic treatment, and they are associated with increased morbidity and mortality.

This has led to growing interest in preoperative optimization programs aimed at improving modifiable risk factors for infection, such as obesity, diabetes, anemia, malnutrition, smoking, and physical inactivity. These programs vary in design and scope, and most are retrospective. Little has been published about their efficacy.

The aim of this project was to implement and evaluate a structured preoperative optimization pathway to reduce infectious and general complications after TJA and to assess its impact on patient health overall.

Methods

This was a prospective case control study examining a multifactorial optimization process coordinated between hospital and primary health care.

Patients in the control group were already on the TJA waiting list and had received conventional preoperative preparation. They were included one week before surgery.

Patients in the intervention group were enrolled during a visit at the outpatient orthopedic clinic after referral from primary health care 6 –12 months before surgery. Initial assessment included blood tests and BMI recording, followed by a primary health care visit within three weeks for review and management. Patients with BMI ≥ 40 were referred to a clinical nutritionist, and those with vitamin D < 50 nmol/L were advised to take supplements. Malnutrition risk was also assessed.

One week before surgery, both groups underwent blood tests and BMI measurements and completed a questionnaire regarding preoperative preparation. Both groups then received the same follow-up.

Data collected included demographics, surgery details, comorbidities (ASA physical status classification), laboratory values, transfusions, hospital stay length, complications, and mortality. Superficial surgical site infections (SSIs), periprosthetic joint infections (PJIs), reoperations, new diagnoses, postoperative health events, and Emergency Room (ER) visits and hospital/Intensive Care Unit (ICU) admissions were recorded.

Results

The control group consisted of 738 of 744 consenting patients included in the study one week before operation. Operations took place between August 2018 and September 2020. The intervention arm consisted of 746 of 1,010 consenting patients included at a median of 307 days before operation. Operations in this group took place between March 2019 and December 2022, with 259 exclusions in cases in which patients declined surgery when offered. Surgery took place during the COVID-19 pandemic in 5% of cases in the control group versus 77% in the intervention group.

The initial results came from the control group as patients in this group underwent surgery earlier. These results revealed an association between obesity and dysglycemia/diabetes and superficial SSI, suggesting potential benefits of risk factor modification. The optimization process within the intervention group resulted in improvement in patient engagement and in metrics such as weight, anemia, HbA1c, and vitamin D.

The baseline characteristics of the two groups one week before operation were similar except that the intervention group had substantially more comorbidities (ASA class 3-4, 32% versus 23%). Despite having more comorbidities, the intervention group presented lower rates of superficial SSI at 6 weeks post-op when adjusted for age, sex, and ASA class (OR 0.64, 95% CI 0.42–0.97). Overall surgical site complications were also lower (11.3% vs. 15.7%; difference 4.5%, 95% CI -8.0 to -1.0).

At one year, superficial SSI was less common in the intervention group (5.9% vs. 7.9%, HR 0.67, 95% CI 0.45–1.01), though this finding was not statistically significant. In the control group, elevated BMI (≥ 30) and HbA1c (≥ 42 mmol/mol) were associated with superficial SSI, but this association was not observed in the intervention group.

At three years, PJI was more common in the intervention group (2.0% versus 1.1%, HR 1.80, 95% CI 0.76–4.30), though the difference between groups was not significant. Most PJIs developed from superficial SSI (80% in the intervention group and 88% in the control group), with 95% of the superficial SSIs in the intervention group and 98% in the control group occurring within six weeks.

Progression from superficial SSI to PJI was more common in the intervention group (27.3%) compared to the control group (12.1%).

At three years, there was no significant difference between the groups regarding new health-related diagnosis and events nor mortality.

Conclusion

A structured preoperative optimization pathway improved modifiable risk factors and reduced short-term superficial SSIs and surgical site complications. However, it did not significantly affect long-term rates of SSIs, PJIs, or overall health and mortality.

External factors, such as the COVID-19 pandemic and transfer of TJA to other facilities, may have influenced results. These findings highlight the need for prospective studies on optimization programs and further evaluation of organizational and practice changes in patient care.

Keywords

Preoperative optimization, total joint arthroplasty, modifiable risk factors, surgical site infection, periprosthetic joint infection

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List of Abbreviations

POMM	Perioperative Medicine and Management
SSAI	Scandinavian Society of Anesthesia and Intensive Care
NIHR	National Institute of Health Research (NIHR)
SSI	Surgical site infections
Superficial SSI	Superficial surgical site infections
ASA	American Society of Anesthesia
TJA	Total joint arthroplasty
MRF	Modifiable Risk Factors
PRT	Progressive resistance training
RCT	Randomized control trial
IQR	Inter quartile range
PJI	Periprosthetic joint infection
MSSA	Methicillin-Sensitive Staphylococcus aureus
MRSA	Methicillin-Resistant Staphylococcus aureus
BMI	Body mass index
WHO	World Health Organization
CDC	Centers for Disease Control and Prevention
NHSN	National Healthcare Safety Network
TRIM	Transfusion-related immune modulation
DAIR	Debridement, antibiotics, and implant retention
Fig	Figure
SD	Standard deviation
OR	Odds ratio
CI	Confidence interval
ICMJE	International Committee of Medical Journal Editors
USA	United States of America
iGAS	Invasive group A streptococci
COVID	SARS-CoV-2
Rstudio R	Foundation for Statistical Computing, Vienna, Austria
OECD	Organization for Economic Cooperation and Development
ER	Emergency room
ED	Emergency department

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List of Original Papers

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals (I–III).

- I. M. Sigurdardottir, M. I. Sigurdsson, Y. Olafsson, S. H. Sverrisdottir, I. Gunnarsdottir, E. L. Sigurdsson, S. Karason. Prevalence of modifiable risk factors in primary elective arthroplasty and their association with infections
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PMCID: PMC9893833 DOI: 10.2340/17453674.2023.8480
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9893833/pdf/ActaO-94-8480.pdf>
- II. M. Sigurdardottir, M. I. Sigurdsson, R. D. Vias, Y. Olafsson, I. Gunnarsdottir, E. L. Sigurdsson, S. Karason. Preoperative optimization of modifiable risk factors is associated with decreased superficial surgical site infections after total joint arthroplasty: a prospective case control study
Acta Orthop 2024 Vol. 95 Pages 392-400
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- III. M. Sigurdardottir, M. I. Sigurdsson, R. D. Vias, Y. Olafsson, I. Gunnarsdottir, E. L. Sigurdsson, S. Karason. Preoperative optimization of modifiable risk factors is associated with decreased superficial surgical site infections after total joint arthroplasty: a prospective case control study.
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Declaration of Contribution

Papers I, II, and III were planned by the doctoral student María Sigurðardóttir (MS) with Professor Sigurbergur Kárason (SK), the supervisor of this project, and with advice from co-instructor Martin Ingi Sigurðsson. MS screened all hospital patient journals and primary health care journals and registered patient data for all patients in the control and intervention groups. MS entered data in the electronic database. Martin Ingi Sigurðsson was a consultant for statistical analysis on Study I, and Rafael Daníel Vias served as a statistical consultant for statistical analysis on Studies II and III. The manuscript was written by MS with guidance from supervisor SK and input from all co-authors.

Disclaimer about the use of artificial intelligence (AI) in thesis preparation: AI was used to rewrite already written text in English. No primary text was written by AI.

The doctoral student, MS, wrote this thesis with guidance from supervisor SK and the doctoral committee.

Prologue

This project started during my studies in Perioperative Medicine and Management (POMM) with the Scandinavian Society of Anesthesia and Intensive Care (SSAI) from 2017 to 2019. Built on decades of MS's clinical experience evaluating patients before operations and recognition of an opportunity to support patients in preparing for operation, was the drive of this study.

1 Introduction

End-stage osteoarthritis is a common and seriously disabling disease affecting 7% of the worldwide population ¹. Total joint arthroplasty (TJA), particularly of the hip and knee, is widely recognized as a highly effective procedure for this disorder that both alleviates pain and immobility and enhances quality of life for affected individuals ². In the United States about 790,000 total knee arthroplasties and 450,000 total hip arthroplasties are done yearly, increasing with the aging population (over 65 years), with the 10-year survival rate of total joint arthroplasty surpassing 95% ².

According to the Organization for Economic Co-operation and Development (OECD), a global forum, the average rate for hip replacements in 2021 was 172 per 100,000 people, while for knee replacements it was 119 per 100,000 people ³.

In 2023, approximately 3.6 million knee replacements were performed globally, as reported by LSI's Global Procedure Volumes Database (Life Science Intelligence) ⁴.

By 2024, more than two million total hip replacements (THR) were carried out annually ⁵.

Although TJA is a highly successful procedure, it can be associated with serious complications. Superficial surgical site infections occur in 1%–10% of TJA, with up to one third of cases progressing into a periprosthetic joint infection (PJI) ⁶⁻⁹.

PJI is considered a disastrous complication of TJA, occurring in 0.5%–2.4% of TJA cases ¹⁰. It often requires repeated surgeries and long-term antibiotic treatment ², leading to prolonged morbidity, increased mortality, a greater burden on patients, and significant costs to healthcare systems and society ¹⁰⁻¹⁴.

Consequently, preoperative optimization of modifiable risk factors (MRFs) before TJA surgery has been growing in demand in recent years, by health care authorities and providers in order to improve the surgical outcomes of TJA, particularly in terms of reducing infections. The aim of preoperative optimization is to decrease postoperative morbidity, improving patient outcomes, and lessen costs ¹⁵.

Preoperative optimization studies have mostly been based on retrospective database reviews ¹³. Thus, there is demand for prospective randomized controlled trials.

There are few prospective comparative trials reporting benefits of these risk mitigation (RM) strategies.

Lau et al. reported in a review on preoperative weight loss. Three randomized controlled trials (RCTs) involving a total of 198 patients were identified. Two studies implemented dietary modification interventions, while one study utilized bariatric surgery. All three RCTs demonstrated significant reductions in body weight and body mass index (BMI) among participants. Furthermore, the intervention groups experienced fewer postoperative complications (odds ratio 2.49, 95% CI 1.08 to 5.74; $P = 0.03$) compared to controls including surgical site complications/infections and PJs¹⁶.

Pegreffi et al. identified in a review, 12 RCTs investigating nutritional supplementation prior to knee arthroplasty, alongside 26 clinical trials and one prospective observational study focused on prehabilitation before surgery. Both prehabilitation and dietary supplementation play a critical role in enhancing surgical resilience by preserving muscle function, accelerating recovery, and improving overall quality of life¹⁷.

Skoffler completed a one-year follow-up¹⁸ after investigating the efficacy of four weeks of preoperative and four weeks of postoperative progressive resistance training (PRT) following total knee arthroplasty a RCT¹⁹. The study of one-year follow up, supports the use of short-term high-intensity resistance training prior to total knee arthroplasty (TKA), demonstrating a long-lasting effect on muscle strength, knee extensor muscle strength (0.5 Nm/kg versus 0.2 Nm/kg, $P = 0.002$), and knee flexor muscle strength (0.3 Nm/kg versus 0.2 Nm/kg, $P = 0.042$). However, this intervention may not produce a significant effect on functional performance (Chair Stand Test (primary outcome), Timed Up and Go Test, walk tests).

1.1 Total joint arthroplasty – a brief history

In 1891, German professor Themistocles Glück performed the first recorded hip arthroplasty using an ivory implant secured with nickel-plated screws on a patient with tuberculosis joint infection. In 1923, American doctor Marius Smith-Petersen tested placing a glass mold over the femoral head, but it shattered upon implantation. In 1953, American surgeon George McKee introduced a metal-on-metal ball-and-socket prosthesis, which ultimately failed due to metal breakage.

In the late 1950s, English surgeon Sir John Charnley, regarded as the father of modern total hip replacement, revolutionized the procedure by using acrylic bone cement—an idea inspired by dental techniques—to improve implant fixation. This

innovation led to the widespread adoption of total hip replacement ²⁰. The first total joint arthroplasty in Iceland was done in 1967 on a hip ²¹.

In 1861, the first resection arthroplasty of a knee due to arthritis was performed by Scottish surgeon Dr. Ferguson in the United States. In 1863, French surgeon Dr. Verneil (Verneuil) executed an operation that involved the implantation of foreign materials into the knee, including a capsule, skin, muscle, and a fat chromicized pig bladder. In 1940, American orthopedic surgeon Dr. Campbell attempted the first hemiarthroplasty, and in 1950 Dr. Walldius from Sweden performed the first bicompartamental knee arthroplasty on a hinge joint, although it was not successful. The groundwork for modern implants was laid in the 1970s by Dr. John Insall, a British surgeon who worked in the United States ²².

1.2 Modifiable Risk Factors (MRF)

Surgical site infections (SSIs) and PJs are significant complications in orthopedic surgeries, particularly following TJA. The association of superficial SSIs originating at the surgical site in the skin and subcutaneous tissue can serve as a precursor to PJI by extending deeper into the fascia and muscles (deep SSI) and to an organ space as a PJI involving the joint and the prosthesis ²³. Understanding the association between SSIs and PJs is crucial for effective prevention and management strategies. Superficial surgical site infections might increase the risk of serious complications such as PJs; this progression is particularly concerning given the complexity and severity of PJs ⁹.

SSIs and PJs are interconnected complications that possess shared risk factors, including both patient-related and surgical risk factors. One such risk factor is prolonged operative time: extended durations of surgery lasting 120 minutes or more have been linked to significantly higher rates of both SSIs and PJs ²⁴. Additional shared risk factors include patient comorbidities ^{9,25} and nutritional status ²⁶. Preventing SSIs is a critical step in reducing the incidence of PJs and thereby improving patient outcomes in joint arthroplasty procedures.

Studies have identified various MRFs for SSIs and PJs. The most common are anemia, diabetes/dysglycemia, obesity, malnutrition, smoking, alcohol consumption, drug abuse, psychological disorders, depression, anxiety, social circumstances, poor dentition, and optimizable comorbidities such as cardiovascular diseases, atrial fibrillation, including anticoagulation treatment, renal diseases, rheumatoid arthritis, Staphylococcus colonization which may be Methicillin Resistant Staphylococcus aureus (MRSA) or Methicillin Sensitive Staphylococcus aureus (MSSA), and possibly the effect of reduced physical capacity ^{13,27-30}. Non modifiable risk factors are inherent and cannot be altered like gender and age.

As postoperative superficial SSI is a risk factor for PJI, it may play a key role to optimize MRFs and comorbidities preoperatively to decrease its occurrence ^{9,27,31}.

PJI is marked by a complex interaction between microbes, primarily bacteria but occasionally fungi, and the host's immune response. A minimal microbial load is sufficient to trigger the infection as causative organisms can adhere to the surfaces of arthroplasty components and form biofilms. Biofilms are known for their significant resistance to a variety of antimicrobial agents and their ability to evade innate immune defenses. The microorganisms responsible for PJI usually originate from the skin microbiome and may be inoculated perioperatively during the implantation procedure. Alternatively, these pathogens can also infect the implant postoperatively through hematogenous dissemination or direct inoculation from neighboring infected tissues ³²⁻³⁷.

The worldwide increase in the number of TJAs may cause increasing numbers of infections, which may in turn produce higher cost affecting health care systems and society more broadly ¹⁴.

Furthermore, if PJIs arise after TJA mortality rate is increased with 5-year mortality rate of 21%–22%, emphasizing the importance of preoperative optimization ¹¹⁻¹⁴.

Obesity

Obesity, or a BMI ≥ 30 (Table 6) is one of the most common risk factors for PJI in TJA ^{38,39}. In a recent study in England, obesity was present in 39% of hip arthroplasties and 57% of knee arthroplasties and presented an increased risk of superficial SSI with increasing BMI ^{40,41}, with a PJI rate of 4.7% among patients with a BMI > 40 ⁴².

Several studies have demonstrated a strong association between elevated BMI and increased risk of PJI. Chen and Lubbecke found infection risks were 2.5 times higher with a BMI > 30 kg/m², 2 times higher with a BMI 35–39.9 kg/m², and 4 times higher with a BMI ≥ 40 kg/m² ^{43,44}. Shohat and Wagner reported a 9% increased risk of PJI per BMI unit above 25 kg/m², with Wagner also highlighting increased wound infection rates ^{45,46}.

Obesity is a pro-inflammatory state that potentially impairs postoperative immune responses and promotes surgical site infections ⁴⁷⁻⁴⁹. Leptin, an adipokine produced by adipose tissue, contributes to inflammation, cartilage degradation, and osteoarthritis, ultimately leading to the need for TJA ^{50,51}. Obese patients also show reduced levels of immune cells such as NK and cytotoxic T cells, with leptin further impairing immune function ⁵².

Obesity often coexists with comorbidities like diabetes, hypertension, and sleep apnea, complicating risk assessment ^{51,53}. Metabolic syndrome comprises a cluster of conditions stemming from insulin resistance and is defined by a BMI > 30 kg/m² plus at least two conditions such as hyperlipidemia, hypertension, or diabetes. Metabolic syndrome is linked to impaired immune function and higher perioperative complications ^{54,55}. Zmistowski reported a significantly higher PJI rate (14.3% vs 0.8%) in patients with uncontrolled metabolic syndrome ⁵⁶.

The risk of PJI has been shown to increase exponentially with BMI. Specifically, a BMI greater than 40 kg/m² increases the risk of infection by 3.3 times, while a BMI greater than 50 kg/m² raises the risk of infection by 21 times ⁵⁷.

Anemia

Anemia may be present in up to 20% of patients undergoing TJA⁵⁸ and is associated with an increased risk of PJI in TJA, occurring at a rate of 4.3% in anemic patients compared to 2.0% in non-anemic patients $p < 0.01$ ^{25,59}. Anemia of chronic disease is a strong independent risk factor for superficial SSI after TJA (OR 3.23, CI 2.70, 3.87, Wald test, $P < 0.001$) ⁶⁰. Anemia leads to decreased hemoglobin levels, compromising oxygen delivery to tissues, impairing tissue repair, and increasing infection susceptibility ^{61,62}. Iron-deficiency anemia can impair immune function by diminishing the efficacy of immune responses, including reduced phagocytic activity and altered cytokine production and decreased humoral immunity by antibodies ^{63,64}. Anemia may also be a surrogate marker for comorbidity that cannot be corrected for ^{65,66}.

Preoperative anemia increases the likelihood of perioperative blood transfusion, which has been linked to a transient immunosuppressive state known as transfusion-related immunomodulation (TRIM); this may raise infection risk by increasing anti-inflammatory cytokines, reducing macrophage cytokine production, and impairing neutrophil and T-cell function ⁶⁷. Although the exact mechanisms remain unclear, TRIM is thought to result from residual white blood cells and immune mediators that accumulate in stored packed red blood cells, even after leukoreduction ^{67,68}.

Diabetes

Diabetes mellitus (types I and II) may be present in up to 20% of patients undergoing TJA) ⁶⁹. The presence of diabetes has been shown to more than double the risk of PJI independent of obesity, with an adjusted odds ratio (OR) of 2.3 (95% CI, 1.1–4.7). Morbidly obese patients with diabetes developed periprosthetic joint infection in 9.8% of cases (95% CI, 4.26% - 20.98%), indicating a synergistic effect

Diabetes mellitus is a well-established risk factor for both superficial SSIs and deeper infections such as PJIs that may develop from superficial SSIs due to immune dysfunction, poor wound healing, poor circulation, and metabolic disturbances, including the following.

Hyperglycemia impairs both innate and adaptive immune responses. It reduces neutrophil chemotaxis, phagocytosis, and microbial killing while also altering T-cell function, which weakens the body's defense against bacterial contamination during and after surgery ^{70,71}.

High glucose levels impair collagen synthesis, angiogenesis, and epithelialization, leading to delayed wound healing and increased infection risk ⁷². Hyperglycemia also promotes bacterial proliferation and biofilm formation at surgical sites ^{73,74}. Diabetic patients are more often colonized with resistant organisms, particularly staphylococcus aureus, further elevating superficial SSI risk ⁷⁵. Tight perioperative glycemic control has been shown to reduce infection rates ⁷⁶.

Microvascular complications of diabetes decrease tissue perfusion and oxygenation, impairing healing and local immune response ⁷⁷. Poorly controlled diabetes, especially with elevated HbA1c levels, is linked to increased PJI and SSI rates ⁷⁸⁻⁸⁰. Current guidelines recommend maintaining perioperative blood glucose levels below 180 mg/dL (10 mmol/L) to minimize infection risk in surgery ⁸¹.

Nutritional status

In orthopedic surgery, nutritional status encompasses three broad categories of conditions, namely undernutrition, micronutrient-related malnutrition, and overnutrition, all of which can impact surgical outcomes ⁸². The most commonly used laboratory markers for assessing nutritional status in orthopedic surgery patients are serum albumin levels < 35 g/L and total lymphocyte count < $1.5 \times 10^9/L$, both of which are associated with poor nutritional status ⁸³. These markers have also been identified as independent risk factors for PJI ²⁵. Given that inflammation may affect nutritional markers such as albumin, these markers should be used in combination with physical patient examination and history ⁸⁴. Additionally, vitamin D deficiency has been found to be more prevalent among patients diagnosed with PJI ⁸⁵.

Malnutrition is recognized as a key MRF in the pre-operative management of TJA and has been linked to several postoperative complications, including PJI, periprosthetic fractures, dislocations, aseptic loosening, anemias, extended hospital stays, higher mortality rates, and increased healthcare costs ⁸⁶.

Malnutrition impairs immune function, with protein and calorie malnutrition in particular weakening both innate and adaptive immunity; this impairs wound healing and increases susceptibility to infection. Deficiencies in micronutrients, zinc, vitamin C, and vitamin D also compromise immune defense mechanisms⁸⁷. Delayed wound healing is associated with insufficient protein intake, with adequate protein intake being essential for collagen synthesis, angiogenesis, and tissue repair. Delayed wound healing increases the risk of SSIs and progression to PJI⁸⁸⁻⁹⁰. Low serum albumin is a widely used marker of malnutrition and has been independently associated with increased risk of PJI. Studies have demonstrated that patients with hypoalbuminemia (< 3.5 g/dL) are at significantly higher risk of postoperative infections^{91,92}.

Obesity may disguise a condition of malnutrition. Obese patients may have micronutrient deficiencies and chronic inflammation that impair immune responses and wound healing, increasing the risk of PJI^{92,93}. Malnutrition has been associated with increased postoperative complications, superficial SSIs, and PJIs in TJA^{94,95}. Nutritional screening and optimization before TJA have been shown to reduce infection risk and improve outcomes⁸⁸. Malnourished patients may be treated with a high-protein diet, adding nutritional supplements^{86,96}. For diabetic and elderly patients, supplements should be low in sugar for glucose control and rich in protein, vitamins, and minerals²⁹.

Smoking

Smoking is a significant risk factor for postoperative wound complications. Current smokers undergoing TJA have significantly increased rates of SSI compared to non-smokers²⁵. In a study by Liang on patients undergoing elective orthopedic surgery, the overall superficial SSI incidence was 3.64%, and tobacco smoking was identified, along with four other independent risk factors, as an independent risk factor of SSI with an OR of 4.2 (95% CI, 2.1–6.4)⁹⁷.

Smoking adversely affects surgical outcomes through multiple mechanisms. Firstly, it impairs wound healing by causing vasoconstriction, reducing tissue oxygenation, and disrupting collagen synthesis. Nicotine and carbon monoxide restrict blood flow, while reduced oxygen tension delays tissue repair^{98,99}.

Additionally, smoking weakens immune response, including both cell-mediated and humoral immune response, by impairing neutrophil, macrophage, and lymphocyte function, which decreases the body's ability to fight bacterial invasion and increases infection risk¹⁰⁰. Cessation of smoking for 4 to 6 weeks pre- and postoperatively has been associated with a reduction in SSI and a 50% reduction in wound complications^{98,101}.

Exercise and functional capacity

Physical strength and stamina are considered important predictors of surgical outcomes, though association with infectious outcomes is not clear ^{30,102}. Moyer identified improvements in pain, physical function and quadriceps strength as well as reduced hospital stay in both hip and knee arthroplasty patients following structured prehabilitation ³⁰, and a six-week exercise program before hip arthroplasty led to 18%–20% gains in muscle strength, better preoperative functional scores, and dramatically lower odds of discharge to rehabilitation facilities (OR 0.27, 95% CI 0.074–0.998) ¹⁰³.

1.3 Preoperative optimization

The rationale behind preoperative optimization in TJA is that in these primarily elective procedures there is ample time to address MRFs preoperatively to engage patients in lifestyle changes, reduce postoperative surgical complications, improve long-term outcomes, and increase cost-effectiveness ^{13,104-106}.

However, studies evaluating the implementation and efficacy of preoperative optimization pathways are limited, despite their importance for evidence-based practice ¹⁰⁷. A recent narrative review of 69 studies identified only three randomized controlled trials and eight prospective cohort studies, highlighting the lack of high-quality evidence in this area ¹³.

A total of 80% of patients undergoing any TJA and 93% of those undergoing revision TJA have at least one MRF, with the most common being morbid obesity (46%), anemia (29%), malnutrition (26%), and diabetes (20%) ³⁸. In addition, failing to optimize patients' MRFs preoperatively was associated with a significantly higher risk of postoperative complications, including SSI, PJI, and pneumonia ³⁹.

A 2020 study by WL Johns, which included data from eight retrospective cohort studies involving a total of 9,915 patients, evaluated the impact of evidence-based preoperative optimization protocols targeting potentially MRFs such as obesity, dysglycemia (poor glycemic control), malnutrition, tobacco and narcotic use, and nasal colonization of MRSA. The implementation of these protocols was associated with a significant reduction in SSIs, with rates decreasing from 2.60% to 0.56% with Relative Risk (RR) of 0.21 (95% CI 0.12–0.37; $P < .00001$). Additionally, these protocols were linked to reductions in hospital length of stay (LOS), mean cost of care, and hospital readmission rates ¹⁰⁸.

Optimization thresholds that should be reached preoperatively to mitigate risk include BMI < 40 kg/m², serum albumin ≥ 3.5 g/dL, HbA1c ≤ 7.5% (58 mmol/mol), hemoglobin > 12.0 g/dL in women and > 13.0 g/dL in men, smoking

cessation, and a $\geq 50\%$ reduction in opioid use at least four weeks before surgery¹³.

However, what, and how many risk factors are addressed, and to what extent, varies between studies¹⁰⁹. Preoperative optimization should be multifactorial to have effect¹¹⁰. Furthermore, the organization of preoperative optimization varies from being entirely hospital-based to taking place in cooperation with primary health care, being carried out within special clinics, or involving a combination of these institutes¹¹¹⁻¹¹³.

Longer-term surveillance and sustained support are essential to maintain the short-term improvements achieved in health outcomes and health-related behaviors. Such ongoing efforts not only reinforce initial gains but also empower patients by leveraging the “teachable moment” to foster greater engagement in their own care¹¹⁴.

1.4 Epidemiology of superficial surgical site and joint infection

1.4.1 Incidence of infection and surgical site complications

The spectrum of postoperative wound complications ranges from minor, self-limiting drainage to more severe outcomes such as persistent wound leakage and full-thickness soft tissue necrosis that requires surgical intervention. If not promptly addressed, these complications—particularly persistent postoperative drainage—can progress to a devastating deep PJI^{115,116}. In joint replacement management, SSI prevention is a key aspect¹¹⁷.

Wound drainage (i.e., effusion) is a surgical site complication that can be serous (clear), serosanguinous (containing blood), sanguineous (primarily blood), or purulent (may indicate infection, culture recommended)¹¹⁸. Postoperative wound drainage affects approximately 1% to 10% of patients undergoing primary TJA^{25,116,119-121}.

Superficial SSI occurrence in the United States is reported to be 1%–2.5%¹²², and this figure increases to 7% in Sweden. Reports vary between 1%–10% of cases⁶⁻⁹.

PJI incidence is 0.5%–2.4% for the Western world^{10,123} and risk may increase by 35-fold from superficial SSI^{8,9}.

1.4.2 Definition of infection

The diagnosis of superficial SSI follows the Centers for Disease Control and Prevention (CDC) criteria, which include documentation of peri-incisional pain or tenderness, localized swelling, erythema, or warmth in the medical record, as well as the initiation of antibiotic therapy recorded in our study ²³.

In contrast, diagnosis of a deep SSI or PJI—which involves deeper structures such as fascia, muscle layers, and the prosthetic joint itself—is made by orthopedic surgeons using validated, evidence-based criteria specific to periprosthetic hip and knee infections. Confirmation of PJI is typically established intraoperatively by obtaining at least five periprosthetic tissue cultures during a debridement, antibiotics, and implant retention (DAIR) procedure, or during a staged revision surgery. In the latter case, a diagnosis of PJI requires at least two positive tissue cultures ¹²⁴.

1.4.3 Microbiology

National surveillance data of surgical site infections for England from April 2018 to March 2023 indicated the total number of hip replacements to be 174,299 (100%) and knee replacements 174,126 (100%). *Staphylococcus aureus* (MSSA) was the most common pathogen in both SSI (Table 1) and PJI (Table 2) following TJA. Coagulase-negative staphylococci were about a quarter of PJI in knees (23.5%) and hips (21.1%) ⁴⁰.

Table 1. Micro-organisms reported as causing inpatient and readmission detected SSIs (superficial SSIs), all surgical categories*, NHS hospitals, England, April 2018 to March 2023

		Hip replacement		Knee replacement	
	Reported causative organism	No.	%	No.	%
Monomicrobial	Meticillin-sensitive <i>S. aureus</i>	37	46.3	35	53.8
	Meticillin-resistant <i>S. aureus</i>	9	11.3	3	4.6
	Coagulase-negative staphylococci	11	13.8	10	15.4
	Enterobacterales	10	12.5	6	9.2
	<i>Pseudomonas</i>	4	5.0	1	1.5
	<i>Streptococcus</i>	3	3.8	1	1.5
	<i>Enterococcus</i>	3	3.8	2	3.1
	Other bacteria	3	3.8	6	9.2
	Fungi including <i>Candida</i> spp.		0.0		0.0
	<i>Acinetobacter</i> spp.	0	0.0	0	0.0
	Anaerobic bacilli	0	0.0	1	1.5
	Anaerobic cocci	0	0.0	0	0.0
	Total monomicrobial	80	100	65	100
Polymicrobial	Gram-positive combinations only	10	43.5	3	14.3
	Gram-negative combinations only	1	4.3	2	9.5
	Gram positive and gram-negative combinations	9	39.1	12	57.1
	Other	3	13.0	4	19.0
	Total polymicrobial	23	100	21	100
	Total cases**	103	100	86	100

* Total cases are specific to this analysis and refers to those with available microbiology information

** Total cases for combined monomicrobial and polymicrobial specimen

Table 2. Micro-organisms reported as causing inpatient and readmission detected SSIs (deep and organ space SSIs), all surgical categories*, NHS hospitals, England, April 2018 to March 2023

		Hip replacement		Knee replacement	
	Reported causative organism	No.	%	No.	%
Monomicrobial	Meticillin-sensitive <i>S. aureus</i>	142	38.0	126	43.4
	Meticillin-resistant <i>S. aureus</i>	18	4.8	12	4.1
	Coagulase-negative staphylococci	79	21.1	68	23.4
	Enterobacterales	75	20.1	25	8.6
	<i>Pseudomonas</i>	10	2.7	10	3.4
	<i>Streptococcus</i>	27	7.2	29	10.0
	<i>Enterococcus</i>	11	2.9	5	1.7
	Other bacteria	6	1.6	10	3.4
	Fungi including <i>Candida</i> spp.	2	0.5	1	0.3
	<i>Acinetobacter</i> spp.	0	0.0	0	0.0
	Anaerobic bacilli	4	1.1	3	1.0
	Anaerobic cocci	0	0.0	1	0.3
	Total monomicrobial	374	100	290	100
Polymicrobial	Gram-positive combinations only	88	46.6	58	41.4
	Gram-negative combinations only	14	7.4	13	9.3
	Gram positive and gram-negative combinations	83	43.9	57	40.7
	Other	4	2.1	12	8.6
	Total polymicrobial	189	100	140	100
	Total cases**	563	100	430	100

* Total cases are specific to this analysis and refers to those with available microbiology information

** Total cases for combined monomicrobial and polymicrobial specimen

One of the largest studies done on PJI in hips and knees, which took place from 2010–2019 at the Mayo Clinic in the United States, showed coagulase-negative Staphylococci to be the most common pathogen in PJI (37%), while Staphylococcus aureus was the second most common (24%) (Table 3) ¹²⁵. A Spanish study showed similar results ¹²⁶. A Chinese study of 35 hospitals identified Staphylococcus aureus (26.5%), coagulase-negative Staphylococcus (14.3%), and MRSA (methicillin resistant staphylococci) being 25.6% ¹²⁷, while a French study presented similar results ¹²⁸.

Ong determined that most infections are diagnosed within two years after operation, or 73.3% hips ¹²⁹, and 77% of knees ¹³⁰. Berbari determined that 59% of PJIs were diagnosed within two years after surgery, while 41% occurred more than two years after surgery ³¹.

Gram-positive staphylococci, whether aureus or coagulase-negative staphylococci like epidermidis, thus seem to be the most common pathogens in PJIs in hip or knee arthroplasty.

Table 3. Isolated microorganisms according to timing of infection

Microorganisms	Total n=2067, n (%)	Early n=442, n (%)	Delayed n=305, n (%)	Late n=1320, n (%)	P Value*
Aerobic Gram-positive bacteria:	1698 (82)	372 (84)	260 (85)	1066 (81)	0.8
Coagulase-negative Staphylococcus species (other than Staphylococcus ludgunensis)	761 (37)	165 (37)	115 (38)	481 (36)	0.9
Staphylococcus aureus complex	497 (24)	140 (32)	79 (26)	278 (21)	<0.001
S. ludgunensis	77 (4)	7 (2)	13 (4)	57 (4)	0.6
Streptococcus species	287 (14)	36 (8)	48 (16)	203 (15)	<0.001
Enterococcus species	155 (8)	38 (9)	20 (7)	97 (7)	0.5
Corynebacterium species	105 (5)	32 (7)	16 (5)	57 (4)	0.03
Aerobic Gram-negative bacteria:	222 (11)	57 (13)	43 (14)	122 (9)	0.01
Enterobacterales	143 (7)	32 (7)	28 (9)	83 (6)	0.2
Pseudomonas species	64 (3)	16 (4)	14 (5)	34 (3)	0.1
Anaerobic bacteria:	262 (13)	72 (16)	35 (11)	155 (12)	0.04
Cutibacterium species	164 (8)	45 (10)	20 (7)	99 (8)	0.1
Other anaerobic bacteria	108 (5)	29 (7)	20 (7)	59 (4)	0.1
Fungi	65 (3)	9 (2)	15 (5)	41 (3)	0.08
Mycobacteria	12 (0.5)	3 (0.7)	6 (2)	3 (0.2)	0.001

* P is for any difference between cells within the row.

1.4.4 Infection treatment

Antibiotic prophylaxis is given intravenously within an hour of surgery. The most common prophylaxis is cephalexin, a first-generation cephalosporine by weight, which is delivered 6 and 12 hours (h) after the start of the operation. In case of antibiotic allergies, vancomycin is recommended due to the high occurrence of clindamycin-resistant staphylococci ¹⁴.

For prevention and treatment of PJI, antibiotic-loaded bone cement (ALBC) is used ¹¹⁷. In cases of PJI, rifampicin is recommended for gram-positive bacteria and fluoroquinolones for gram-negative bacteria. PJI treatment becomes more complicated due to possible biofilm formation on the prosthesis surface within four weeks, which causes resistance to antibiotics in the host's immune system. The biofilm is made of bacterial accumulation embedded in organic polymer matrix, including proteins, DNA (deoxy ribonucleic acid), and polysaccharides, which adhere to the prosthesis surface ¹³¹. Antibiotic tolerance may develop during treatment, necessitating prolonged antibiotic therapy, particularly when the prosthesis remains in place. In cases managed with DAIR—typically performed within six weeks of the index operation—antibiotic therapy can extend up to three months or longer depending on the clinical response. In contrast, two-stage revision procedures, which involve removal of the infected prosthesis and placement of an antibiotic-loaded spacer, are followed by a course of systemic antibiotics typically lasting six weeks or more, based on intraoperative findings and microbiological results. After completion of antibiotic therapy, reimplantation of a new prosthetic joint is performed ¹³². Antibiotic treatment is managed through collaboration between infection specialists and orthopedic surgeons to ensure optimal eradication of infection and favorable surgical outcomes.

In a study by Longo of 12 articles on results following DAIR operations of early infections and acute hematogenous infections, good results occurred in 55% to 90% of cases (mean 71%) ¹³³.

Six weeks after the primary operation, one-step and two-step revisions are performed to treat PJIs. During one-step operations, the prosthesis is removed and replaced with a new prosthesis during the same operation, if conditions allow, and only in selected cases. In two-step operations, the prosthesis is removed for a spacer, and antibiotic treatment follows, usually for six weeks or longer if needed. A new prosthesis is implanted when the joint is deemed infection-free ¹¹⁷.

1.4.5 Biofilms

Biofilm formation on the surface of orthopedic implants plays a critical role in the pathogenesis of PJI as it protects bacteria from both antimicrobial agents and the host immune system ¹³⁴. Biofilm is composed of bacteria, extracellular DNA, proteins, and polysaccharides, all of which adhere to the prosthetic surface. Staphylococci, particularly *Staphylococcus aureus* and *Staphylococcus epidermidis*, are the primary pathogens in orthopedic PJI and are capable of producing robust biofilms, contributing to bacterial persistence and antibiotic resistance.

Biofilm development follows four distinct stages:

Adherence – initial bacterial attachment to the biomaterial surface.

Accumulation – bacterial cell-to-cell adhesion promoting colony formation.

Maturation – secretion of a protective extracellular glycocalyx matrix that anchors the bacteria and shields them from immune responses.

Detachment – dispersal of bacteria from the biofilm surface, enabling colonization of nearby tissue and formation of new biofilms ¹³¹.

Mature biofilm is typically established within four weeks, at which point infection becomes significantly more difficult to eradicate, often necessitating surgical intervention or prosthesis removal ^{131,135}. Rifampin has demonstrated effectiveness against staphylococcal biofilms and may be used in combination therapies for these infections ¹³⁴. However, eradication of biofilm without implant removal remains a significant challenge, and further research is needed to develop effective biofilm-disrupting strategies ¹³¹.

2 Aims

This work implements a patient pathway for pre-operative optimization of MRFs prior to operation in order to minimize postoperative infections and complications after TJA of hips and knees, in cooperation of hospital and primary health care. The study also evaluates the long-term effects of such a program on patients' general health.

These aims are motivated by the fact that there are very few prospective studies on preoperative optimization and calls in the current literature for further research on this. Additionally, the small size and relative seclusion of Icelandic society and a health care system where all registrations in hospital and primary health care journals are dependent on social security numbers allows thorough follow up of patients, enabling reliable results.

Study I

The aim of this study was to investigate the prevalence of MRFs for superficial SSI in patients undergoing primary TJA who receive standard preoperative preparation, and to evaluate the association between these risk factors and the incidence of postoperative infections.

Study II

The aim of this study was to evaluate the impact of a structured preoperative patient pathway aimed at optimizing MRFs for their prevalence and their change to assess whether this intervention is associated with a reduced incidence of superficial SSIs following primary TJA.

Study III

The aim of this study was to prospectively evaluate the impact of a preoperative optimization program on long-term postoperative infectious surgical complications and to assess whether it led to sustained improvements in general health compared to conventional preoperative preparations.

3 Material and Methods

3.1 Study design and settings

Studies I–III were all approved by the Science Committee of the Capital Area's Primary Health Care and University of Iceland and by the Icelandic National Bioethics Committee (case number: VSN-18-098). All three studies were registered at ClinicalTrials.gov (NCT05399186).

In 2017, planning began for a prospective case-control study aimed at preoperative optimization of MRFs by implementing a patient pathway involving cooperation between hospital and primary health care. The main risk factors considered in the research included anemia, diabetes mellitus/dysglycemia, obesity, malnutrition, and smoking.

The study also included a questionnaire to assess the patient's awareness of MRFs and if they tried to influence them prior to operation.

The primary objective was to mitigate the risk factors of anemia, diabetes, obesity, malnutrition, and smoking and to encourage motion prior to surgery, thus potentially reducing the risk of postoperative complications such as infections and possible health effects. All planned to happen in cooperation with primary health care, including specialist consultations when indicated.

Support was secured from both hospital and primary health care directors, and a formal agreement was made with primary health care physicians to promote collaboration. Subsequently, a series of informational meetings were held at various primary health care centers. A patient optimization pathway was structured and implemented through coordinated efforts involving multiple stakeholders. Clear lines of communication were established among orthopedic services, primary health care physicians, the hospital's orthopedic outpatient clinic, the preoperative assessment center, the clinical nutrition department, and hospital specialist outpatient services. Follow up after surgery was also decided (Figure 1).

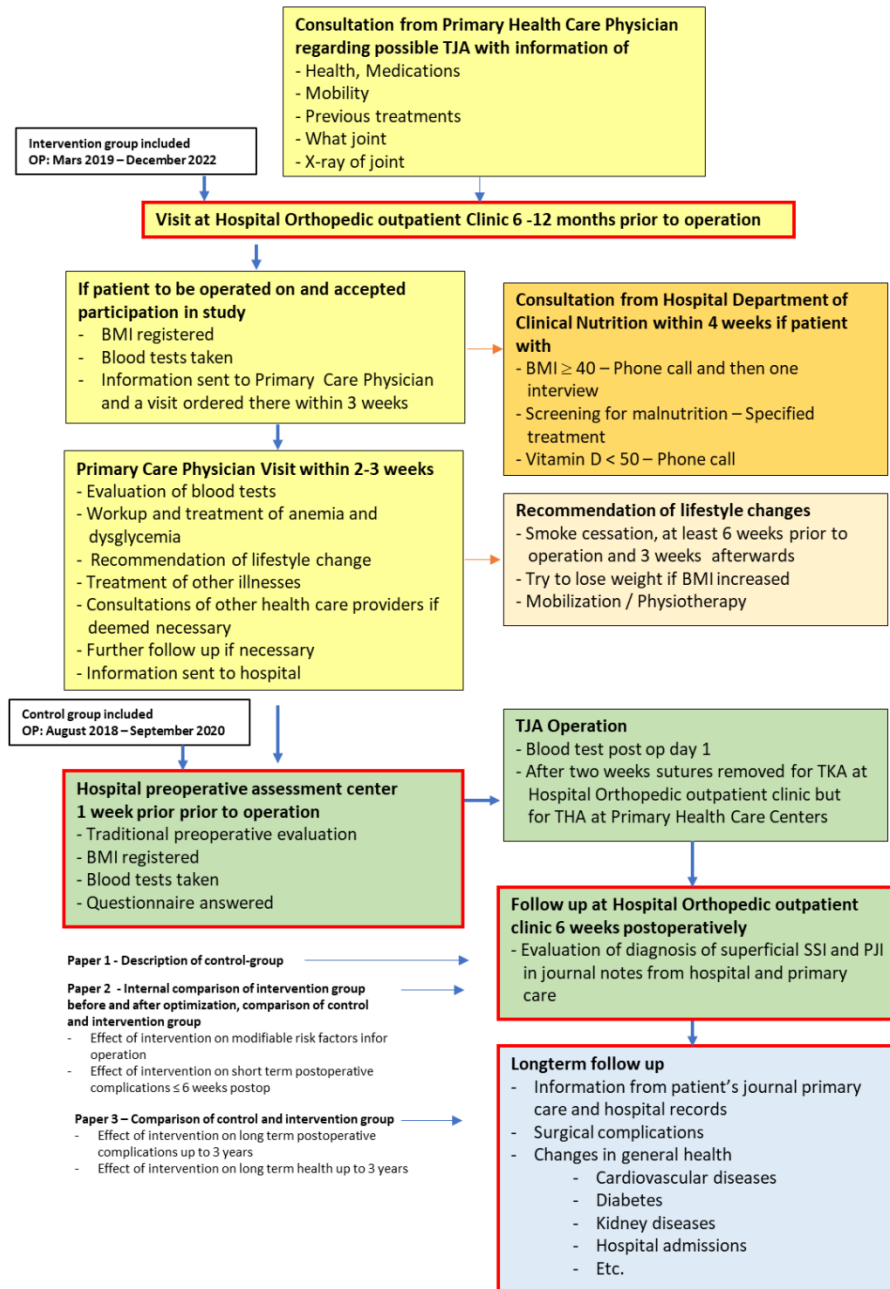


Figure 1. Study organization of patient flow, points of registrations and formation of papers

All three papers were based on a prospective, single-center study at Landspítali National University Hospital in Reykjavík, Iceland, and involved patients undergoing primary TJA. The intervention group received preoperative optimization through primary health care.

The control group was enrolled between August 2018 and September 2020, and surgery took place during that time. The intervention group was enrolled from January 2019 to January 2021, with surgeries taking place from March 2019 to December 2022.

Control group patients were recruited at the hospital's preoperative clinic one week before surgery after receiving preoperative advice without follow up. Blood tests, BMI, and questionnaires were completed at that time during recruitment (Paper I).

Intervention group patients were enrolled at the time of surgical decision (6–12 months pre-op) and referred from primary health care. After initial testing and BMI registration, they received a primary health care follow up within three weeks focusing on MRFs (e.g., anemia, diabetes, obesity, nutrition, smoking, activity), with specialist referrals if needed.

Paper I describes the prevalence of MRFs and their association with infectious complications in a patient group receiving conventional preoperative preparation.

Paper II assesses the effect of optimization by comparing surgical outcomes—particularly infections—between groups six weeks post-op.

Paper III presents long-term follow-up (up to five years) results with a cutoff for superficial SSIs at one year and for PJI at three years, focusing on surgical complications and overall health.

The study center was Landspítalinn – The National University Hospital of Iceland in Reykjavík. Health care in Iceland is funded by taxes, with an official sector that includes Landspítali and most of the primary health care, and a private sector where agreements are made between the government and various health care providers.

Landspítali is a 610-bed tertiary care center stationed in two areas of the capital. The orthopedic department has 30 beds. Patients are admitted for elective arthroplasty from the capital area and the countryside. About 2,000 orthopedic operations take place per year, of which approximately 700 to 800 are arthroplasties.

Table 4. A summary of the patient population studied in this thesis and the main outcome measures.

	Study I	Study II	Study III
Included patients	TJA operations willing to participate in study Control group	TJA operations willing to participate in study Intervention group	Control and intervention group 1484
Nr. of patients	738	Control 738 Intervention 746	Control + Intervention = 1484
Study period	2018 to 2025 Control	2018 to 2025 Control Intervention	2018 to 2025 Control Intervention
Study design	Descriptive prospective study	Prospective case control study six weeks follow up after surgery	Prospective case control study, long term follow-up
Outcome measures	Superficial SSI infection incidence and primary joint infection $\leq 6w$ Prevalence of MRF	Superficial SSI infection incidence and primary joint infections $\leq 6w$ Change in MRF following preop optimization	Superficial SSI infection incidence up to one year Primary joint infections up to three years Long term health effect of intervention

3.2 Patient selection

Control and Intervention Groups

All adult patients (≥ 18 years) scheduled for primary TJA of the hip or knee at Landspítali—The National University Hospital of Iceland were invited to participate in the study.

Control Group

The control group included patients already on the surgical waiting list who had undergone standard preoperative preparation. These patients were recruited approximately one week prior to surgery. Between August 2018 and September 2020, 744 patients were invited to participate during their visit to the hospital's preoperative assessment clinic. Of these, 738 patients were enrolled and underwent surgery during the same period.

Intervention Group

Patients referred from primary health care to the hospital's outpatient clinic 6–12 months before surgery were offered participation at the time of surgical decision. A total of 1,010 patients agreed to join the intervention group between January 2019 and January 2021, following a pilot phase. Their surgeries took place between

March 2019 and December 2022, with some delays due to the COVID-19 pandemic.

Preoperative Assessment and Optimization

Control Group: Blood tests were conducted one week before surgery. BMI was recorded, and patients completed a questionnaire covering weight changes, anemia treatment, nutrition, smoking, and any specialist consultations.

Intervention Group: Patients underwent blood testing at the time of surgical decision and were scheduled for a follow-up visit with a primary health care physician within three weeks. MRFs were addressed through preoperative optimization, which included:

- 1) Treatment of anemia and diabetes to target levels, counseling on nutrition and weight loss for patients with obesity, prescription of physical activity and physiotherapy to enhance mobility from primary health care providers
- 2) Nutritional consultation for patients with BMI ≥ 40 kg/m² or vitamin D levels < 50 nmol/L by Landspítali University Hospital, Department of Clinical Nutrition. Smoking cessation support was offered by primary health care providers.

Repeat blood tests and a follow-up questionnaire were completed one week before surgery, BMI was recorded, and patients completed a questionnaire covering weight changes, anemia treatment, nutrition, smoking, motion, and any specialist consultations.

Follow-Up and Outcomes

All patients underwent TJA (hip or knee) on their scheduled surgery day. Both groups were followed long-term until the occurrence of defined outcomes, with comparisons made regarding the incidence of superficial SSIs, PJIs, and other long-term health effects to evaluate the impact of preoperative optimization.

Patients were operated for total joint arthroplasty of the hip or knee on the day of arrival at the hospital.

3.3 Procedure

Thromboprophylaxis with low molecular weight heparin began the night before surgery and continued for up to 10 days postoperatively. Prophylactic antibiotics were administered within one hour before incision and repeated at two and six hours post-incision. Spinal anesthesia was the preferred method, with general

anesthesia reserved for specific cases. Tranexamic acid was given intraoperatively to reduce blood loss. For pain control, ropivacaine was locally infiltrated, particularly in knee arthroplasty cases. Surgical drains were generally avoided.

Following surgery, patients were transferred to the postoperative recovery unit and then to the orthopedic ward once stable, typically on the same day. Most patients were discharged after an overnight stay. Suture clips were removed after two to three weeks, with follow-up taking place in primary health care for hip arthroplasties and at the hospital for knee procedures. A six-week postoperative follow-up was offered to all patients at the orthopedic outpatient clinic during the meeting with the surgeon. In cases of postoperative complications, patients or healthcare providers were instructed to contact the orthopedic outpatient clinic or the on-call orthopedic resident.

3.4 Data collection (Clinical variables, definitions and follow up)

In Studies I, II and III, clinical variables included age, gender, weight, smoking status, comorbidities, type of surgery and anesthesia, ASA (American Society of Anesthesiologists) classification (Table 5) ¹³⁶, laboratory values, blood transfusions, and length of hospital stay. BMI was classified according to the World Health Organization (WHO) definition (Table 6) ⁵³, with obesity defined as $\text{BMI} \geq 30 \text{ kg/m}^2$ ¹³⁷. Further stratification from the surgical literature categorize obesity into three classes: severe obesity ($\text{BMI} \geq 35$), morbid obesity ($\text{BMI} \geq 40 \text{ kg/m}^2$), and extreme or super obesity ($\text{BMI} \geq 50 \text{ kg/m}^2$) ¹³⁸.

Table 5. American Society of Anesthesiologists Physical Status Classification System.

ASA Physical Status Classification	Definition	Examples
ASA 1	A healthy patient	A fit, nonobese, nonsmoking patient with no underlying disease and good exercise tolerance
ASA 2	A patient with systemic disease that is mild	A patient with no functional limitations and a well-controlled disease, obesity with a BMI 30-40, frequent social drinking, or current cigarette smoking
ASA 3	A patient with systemic disease that is severe but not life-threatening	A patient with some functional limitation due to poorly controlled moderate/severe disease(s), morbid obesity with BMI 40 or above, substance abuse, end-stage renal disease undergoing regular dialysis, implanted pacemaker, or remote history of coronary or intracerebral ischemic event (not within the past 3 months)
ASA 4	A patient with "severe systemic disease that is a constant threat to life"	A patient with substantial functional limitations due to severe, life-threatening diseases, such as coronary or intracerebral ischemic event within the past 3 months, severe end-organ dysfunction (cardiac, pulmonary, renal), ongoing coagulopathy, and shock states
ASA 5	A comatose patient who is "not expected to survive without the operation"	Ruptured aneurysm, multisystem trauma, or extensive intracranial hemorrhage with mass effect
ASA 6	A brain-dead patient whose organs are being procured for transplantation into another patient	

Table 6. World Health Organization Classification of Obesity

Classification	BMI (kg/m ²)	Risk of comorbidities
Underweight	<18.50	Low (but risk of other clinical problems increased)
Normal Range	18.50-24.99	Average
Overweight:	≥25.00	
Preobese	25.00-29.99	Increased
Obese class I	30.00-34.99	Moderate
Obese Class II	35.00-39.99	Severe
Obese Class III	≥40.00	Very severe

Diabetes status was determined based on a preoperative diagnosis or HbA1c levels. Patients without a prior diagnosis of diabetes were classified as having dysglycemia if HbA1c levels were between 42–47 mmol/mol, and as having undiagnosed diabetes if HbA1c exceeded 47 mmol/mol. Preoperative blood glucose and postoperative day 1 (POD 1) morning blood glucose levels were also measured for all patients.

Preoperative anemia was defined according to the WHO criteria as a hemoglobin concentration of < 120 g/L in women and < 130 g/L in men ¹³⁹. Anemia was further classified as mild (110–119 g/L in women or 110–129 g/L in men), moderate (80–109 g/L), or severe (< 80 g/L), with no cutoff for both sexes. Patients at risk of malnutrition were identified by low serum albumin levels < 35 g/L or reduced lymphocyte count < 1.5x10⁹ ⁸³. Vitamin D deficiency was defined as a serum 25-hydroxyvitamin D (25-OH-D) concentration of < 50 nmol/L ¹⁴⁰.

The questionnaire gathered information about smoking and level of physical activity. Patients who smoked previously were asked when they quit (> 1y ago, > 6m, > 6w, and < 6w ago).

Preoperative physical activity, including prescribed physical activity, was assessed according to the recommendations of the Swedish Professional Associations for Physical Activity and included activities provided by primary health care services and physiotherapy ¹⁴¹. Physical activity was categorized into two frequency classes: 0–2 times per week and 3–5 times per week, with durations per exercise session of 0, 0–20, 20–40, 40–60, and > 60 minutes.

The first follow up in the control group occurred in the primary health care setting 2–3 weeks postoperatively for suture removal. In the intervention group, follow up for hip TJA occurred 2–3 weeks in the primary health care, and for knee TJA at the hospital orthopedic outpatient clinic given the increased risk for superficial SSI in knee patients. Patients outside the capital area were referred to the hospital outpatient clinic in cases of complications during follow up. At six weeks post

operation, all patients were offered a visit to the hospital orthopedic outpatient clinic. No patient was lost in the follow up stage.

All patient records from both hospital and primary health care were reviewed to identify diagnoses of superficial or deep SSIs, as well as other postoperative complications. Superficial SSIs were diagnosed according to CDC criteria based on clinical signs including peri-incisional pain, tenderness, swelling, erythema, localized heat, and the presence of antibiotic prescriptions documented in the medical records ²³.

Deep SSIs or PJIs involving fascia, muscle layers, and prosthetic components were diagnosed by orthopedic surgeons using validated criteria. Diagnosis was confirmed by obtaining five periprosthetic tissue cultures during a DAIR procedure or during a formal PJI revision surgery, in accordance with the 2018 definition of PJI by Parvizi et al ¹²⁴.

In Study III, patient records from both primary health care and hospital were reviewed to identify new postoperative health-related diagnoses such as comorbidities, hypertension, arrhythmia, ischemic heart disease, heart failure, aortic stenosis, diabetes, obstructive lung disease, worsening of kidney function, cancer, including prescription of GLP-1 agonists, and an increase in BMI and anticoagulation. In addition, the records were reviewed to identify new health-related events that had occurred postoperatively such as myocardial infarction, cardiac arrest, pneumonia, deep vein thrombosis, pulmonary embolism, and transient ischemic attack.

Information was gained from the hospital analytical data division regarding visits to the emergency department, admissions to the hospital, and admissions to the ICU that occurred postoperatively.

Databases from Studies I and II, including health-related diagnoses or comorbidities and health-related events preoperatively, were extended with follow up until time to event, with a cutoff at three years, including primary joint infections more than 6 weeks post-operation, DAIR/PJI. Health decline was registered as a worsening of preexisting comorbidities or a new diagnosis post-operation. Patients' comorbidities and events were measured preoperatively and postoperatively to measure the effects of preoperative optimization.

3.5 Intervention group, optimization of patient pathway and implementation

The grounds for these studies were laid in 2017 to utilize patients' waiting time before TJA to improve MRFs.

Information meetings were conducted in primary health care centers across the capital area, as well as the southern, southwestern peninsula, western, and Westfjords regions of Iceland, with all areas willing to participate in the study. Implementation was initiated following the design of the preoperative optimization patient pathway (Fig 1).

Patients were invited to participate in the study at the hospital outpatient clinic following referral from the primary health care physician. Upon their acceptance, initial blood tests were performed. Subsequently, the patient was scheduled for a follow-up consultation with their primary health care physician within three weeks, typically 6–12 months prior to the planned operation. The results of the blood tests were evaluated to determine whether additional tests, treatments, or specialist consultations were necessary, with a particular focus on obesity, glycemic control, anemia, nutritional status, smoking cessation, and physical activity.

Hospital-based clinical nutritionists contacted patients with a BMI ≥ 40 kg/m² via phone and offered a personal consultation, during which general dietary advice was provided. Patients with vitamin D levels < 50 nmol/L were also contacted with one phone call, during which they received individualized daily dosing recommendations aimed at reaching a target serum level of 75 nmol/L, ideally at least three months prior to surgery ¹⁴².

Risk of malnutrition was assessed using a validated screening tool ¹⁴³ (Figure S1 in the Appendix). Patients identified as being at risk of malnutrition were offered consultation with a clinical nutritionist.

Patients came for re-evaluation at the preoperative assessment clinic the week before the arthroplasty surgery date. They answered a questionnaire on their apprehension of the preoperative optimization attempt, trying to affect health factors like weight, motion, use of physical activity, nutrition, smoking, and anemia treatment. Visits to primary health care centers and specialists' consultation visits and their satisfaction level with hospital and primary health care services.

3.6 Microbiology

Culture results were registered from patient records in Studies I–III. Cultures were taken in 49% of superficial SSI cases in the control group and in all cases of DAIR

and PJI or (100%). Five tissue cultures were taken in every DAIR and PJI operation for both groups, and two positive tissue cultures of the same pathogen were needed for diagnosis of joint infection. If tissue cultures were negative (i.e., due to previous antibiotic treatment), a clinical diagnosis was made by both an infection specialist and orthopedic surgeon following DAIR or PJI operations. A fistula communicating with the joint is always considered a joint infection ¹²⁴. In the intervention group superficial SSI cultures were taken in 48% of cases and in 100% of cases of DAIR and PJI (Table 14).

3.7 Outcome variables

Study I

The primary outcome of Study I was to determine the prevalence of MRFs among Icelandic patients undergoing TJA, which had not been previously described.

The secondary outcome was to investigate whether these MRFs were associated with the occurrence of superficial SSIs.

Study II

The primary outcome of Study II was to evaluate change in MRFs following implementation of optimization before arthroplasty surgery. This research pathway, developed in collaboration with both primary health care and hospital teams, aimed to assess the impact of preoperative optimization on MRFs such as obesity, diabetes, anemia, malnutrition, smoking, and physical activity.

The secondary outcomes focused on evaluating the potential effects of managing these MRFs and whether this intervention could influence the risk of superficial SSIs and joint infections following TJA compared to a conventional control group. These outcomes were assessed after a six-week follow-up period.

Study III

The primary outcome of Study III was the gathering of the incidences of superficial SSIs and PJIs with a cutoff at one year for superficial SSIs and at three years for PJIs to determine if preoperative optimization was associated with superficial SSI and PJI incidence in the long run. The one year cutoff for superficial SSI was chosen as all superficial infections and complications from the surgical wound should be over by that time. The three-year cutoff for PJI was chosen in accordance with recruitment of patients in follow up.

The secondary outcome was whether preoperative optimization of MRFs had any beneficial effects on health-related diagnoses or patients' comorbidities, such as

new postoperative long-term health diagnoses or worsening of hypertension, arrhythmia, including anticoagulation, ischemic heart disease, heart failure, aortic stenosis, diabetes, obstructive lung disease, worsening of kidney function, cancer, including prescription of GLP-1 agonists, and increase in BMI. In addition, acute health-related events that occurred postoperatively were recorded, including myocardial infarction, cardiac arrest, pneumonia, deep vein thrombosis, pulmonary embolism, and transient ischemic attack.

3.8 Statistics

Statistical significance was set at $\alpha = 0.05$ across all studies. Reference values for significance were 0 for confidence intervals of differences and 1 for odds ratios. Patient demographics were described using median and interquartile range or mean and standard deviation for numerical variables and frequencies with percentages for categorical variables.

Study I (Risk Factor Analysis): Missing data was assumed to be missing at random. Univariate logistic regression assessed associations between five MRFs (pre-operative anemia, HbA1c ≥ 42 mmol/mol, BMI ≥ 30 , smoking, vitamin D < 50 nmol/L, and physical activity) and postoperative superficial SSI occurrence, estimating odds ratios with 95% confidence intervals. As this was a descriptive study, no power analysis was conducted. Analyses were performed using R version 1.3.1093 (R Foundation for Statistical Computing, Vienna, Austria).

Study II (Intervention Trial): Sample size calculations were based on preliminary analysis of the first 100 control patients, identifying 8% with superficial SSI. We estimated that risk factor optimization could reduce this to 4%, with 550 patients needed per group, though 1,000 patients were targeted. Data normality was assessed using the Shapiro–Wilk tests. In cases of non-normal distributions, bias-corrected accelerated bootstrap confidence intervals were computed for continuous data comparisons, while the Newcombe Score method was used for proportion differences. Univariate logistic regression examined associations between patient characteristics and superficial SSI in the intervention group. Multivariable logistic regression assessed intervention effects while adjusting for age, sex, and ASA classification. Missing data was below 3% for clinical variables but ranged from 2.4%–65.9% for questionnaire responses. Analyses were performed using R version 4.2.2.

Study III (Long-term Outcomes): Competing risk methodology was employed as the primary analytical approach, recognizing that death precludes observation of infections and other outcomes. Fine-Gray subdistribution hazard models were fitted

for SSI and PJI outcomes to estimate intervention effects, treating death as a competing risk and adjusting for sex, age category, and ASA score. Cumulative incidence functions were estimated using the Aalen–Johansen estimator, with Gray's test comparing curves between groups. For count outcomes involving cumulative illness diagnoses and serious health events, negative binomial regression calculated incidence rate ratios with offset terms for variable follow-up duration, assuming patients returned to baseline risk after each healthcare encounter. Both crude and adjusted models were fitted, controlling for age, sex, and ASA score. Kaplan–Meier survival analysis with log-rank tests evaluated mortality outcomes. Univariate logistic regression and Fisher's exact tests assessed associations between MRFs and outcomes, stratified by treatment group. Missing data was negligible for primary clinical variables (BMI: 0.07%, all others: 0%). Last observation carried forward was used for survival curve visualization, but no other imputation methods were employed. Analyses were performed using R version 4.5.0.

4 Results

Inclusion of patients in control and intervention groups

Control group

Out of 744 patients who agreed to participate in the study, 738 were included in the control group analysis. Six patients were excluded: two due to contraindications for operation and four due to operation on another joint during the inclusion period.

Intervention group

Out of 1,010 patients who agreed to participate in the study, 746 were included in the intervention group analysis. A total of 259 patients declined undergoing operation when offered, one patient was included twice, and four operations contraindicated (Figure 2).

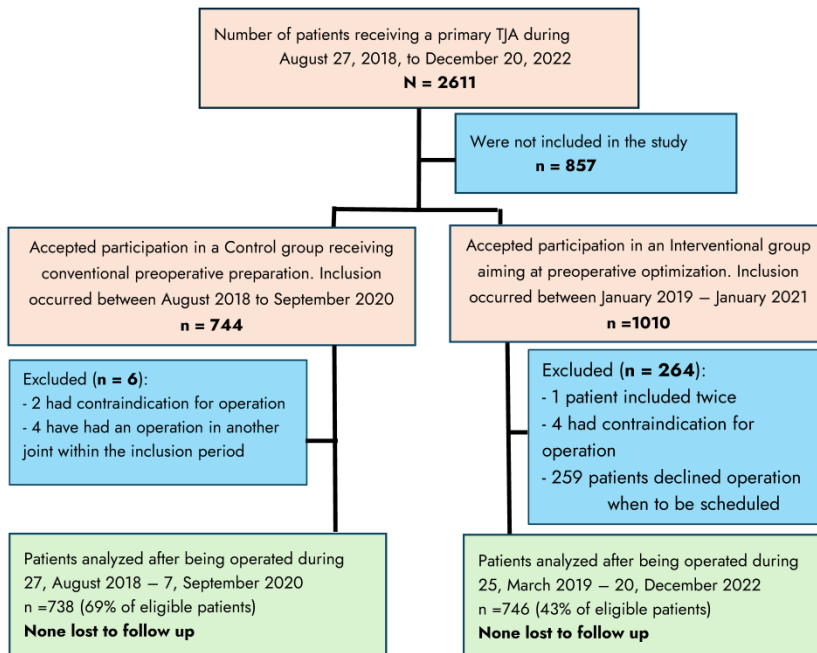


Figure 2. Patient inclusion during the study time, being operated on and followed up

4.1 Effect of preoperative optimization on Modifiable Risk Factors in the Intervention group

Patient characteristics at the time of the operation decision and one week preoperatively (7) were the two time points when data on MRFs was collected. In the interval between these time points, they underwent optimization of MRFs.

The patients had a mean (SD) wait time to operation of 355 days (223). CI is 95% CI in this thesis. There was a slight decrease in the mean (SD) BMI from 31.4 (5.8) to 31.0 (5.4) (difference -0.4, CI -0.6 to -0.3), most in those with a BMI ≥ 40 at decision of operation or 8.4% of the patients, reduced to 6.0% a week before operation (difference -2.4, CI -3.9 to -1.0). Patients with a BMI ≥ 40 received weight loss consultations in 90% of cases (40 from clinical nutritionists at the hospital, 11 in primary health care, and 4 in weight loss centers; 6 received bariatric surgery).

Improvements were also observed in several health markers from decision for operation till one week preoperatively, values are count (%) unless otherwise specified. Anemia underwent a slight reduction from 55 (7.4) to 44 (5.9) (difference -1.5, CI (-3.4 to 0.4), while HbA1c mmol/mol improved, values are mean (SD), 38.2 (7.6) to 37.8 (7.3) (difference -0.4, CI -0.7 to -0.1). Albumin mean (SD) decreased from 45 (2.7) to 43.4 (2.7) (difference -1.6, CI (-1.8 to -1.4). Albumin < 35 g/L had one patient (0.1) on decision and one at time of operation (0.1), (difference 0.0, CI -0.6 to 0.6) one week before operation. Vitamin D levels increased, with 92% of patients with vitamin D deficiency receiving consultation and raising their mean vitamin D levels from 36 to 71 nmol/L by one week before operation (difference 4.7, 95% CI 28.6 to 41.5) (Table 7).

Table 7. Intervention group patient characteristics (N = 746) at 2 timepoints, at decision of operation and 1 week prior to it. The difference between the 2 timepoints is calculated between means when presented, otherwise between proportions (shown in brackets) and is presented with 95% confidence interval. Values are count (%) unless otherwise specified.

Patient characteristics of intervention group	At decision of operation	Missing	1 week prior to operation	Missing	Difference [CI]
Days of wait ^a			355 (223)	0 (0)	
Age ^a			67.9 (9.7)	0 (0)	
Female sex			414 (55)	0 (0)	
BMI ^a	31.4 (5.8)		31.0 (5.4)		-0.4 [-0.6 to -0.3]
< 18.5	1 (0.1)		1 (0.1)		0.0 [-0.5 to 0.5]
18.5–24.9	94 (13)		102 (14)		1.1 [-0.3 to 2.5]
25–29.9	228 (31)		231 (31)		0.4 [-1.8 to 2.6]
30–34.9	236 (32)		241 (32)		0.7 [-1.8 to 3.1]
35–39.9	124 (17)		126 (17)		0.3 [-2.0 to 2.5]
40–44.9	46 (6.2)		39 (5.2)		-0.9 [-2.5 to 0.6]
45–49.9	15 (2.0)		6 (0.8)		-1.2 [-2.4 to -0.3]
≥50	2 (0.3)		0 (0)		
Nutritionist consultation ^b					
BMI ≥40	63 (8.4)		45 (6.0)		-2.4 [-3.9 to -1.0]
Blood tests					
Hemoglobin, g/L ^a	141.4 (12.8)	1 (0.1)	140.9 (12.6)		-0.6 [-1.2 to 0.1]
Anemia	55 (7.4)	1 (0.1)	44 (5.9)	0 (0)	-1.5 [-3.4 to 0.4]
mild	46 (6.2)		38 (5.1)		-1.1 [-3.1 to 0.9]
moderate	9 (1.2)		6 (0.8)		-0.4 [-1.5 to 0.6]
severe	0 (0)		0 (0)		0.0 [-0.5 to 0.5]
Creatinine, μmol/L ^a	82.7 (41.6)	2 (0.3)	83.9 (47.7)		1.1 [0.1 to 2.2]
Glucose, mmol/L ^a	6.0 (1.3)	2 (0.3)	6.4 (1.5)	1 (0.1)	0.3 [0.2 to 0.4]
HbA1c, mmol/mol ^a	38.2 (7.6)	3 (0.4)	37.8 (7.3)	7 (0.9)	-0.4 [-0.7 to -0.1]
HbA1c for non-DM patients		2 (0.3)		7 (1.1)	
42–47 mmol/mol	46 (6.2)		49 (6.6)		0.5 [-1.7 to 2.7]
> 47 mmol/mol	6 (0.8)		8 (1.1)		0.3 [-0.7 to 1.4]
Albumin, g/L ^a	45.0 (2.7)	3 (0.4)	43.4 (2.7)	10 (1.3)	-1.6 [-1.8 to -1.4]
Albumin < 35 g/L	1 (0.1)	3 (0.4)	1 (0.1)	10 (1.3)	0.0 [-0.6 to 0.6]
Lymphocytes < 1.5x10 ⁹ /L	106 (14)	1 (0.1)	79 (11)	1 (0)	-3.6 [-6.3 to -1.0]
Vitamin D, nmol/L ^a	84.7 (34.5)	5 (0.7)			
Nutritionist consultation ^b					
Vitamin D < 50 at decision, nmol/L ^a	36.2 (9.3)		70.9 (28)		34.7 [28.6 to 41.5]

^a Values are mean (SD)

^b Individuals that had BMI ≥ 40 and those with vitamin D < 50 on decision for operation received a nutritionist consultation on decision for operation. The change in number of patients with BMI ≥ 40 is shown at the 2 different timepoints and the change in mean vitamin D for the group that had < 50 nmol/L at decision of operation.

4.2 Modifiable Risk Factor Incidence in the Control and Intervention groups one week preoperatively

Mean patient age (SD) was 67.9 (9.7) years in the intervention group and 66.7 (8.8) years in the control group (difference 1.2 years, CI (0.3 to 2.2)). Gender distribution was similar between groups, with females comprising 55% of the intervention group and 57% of the control group.

The frequency of hip and knee prostheses was comparable between the control and intervention groups, with knee prostheses accounting for approximately two thirds of all cases (Table 8).

Body Mass Index

Body mass index (BMI), was evenly distributed between weight groups at one week before operation in the control and intervention groups, with 52% of patients in the control group having a BMI ≥ 30 kg/m² compared to 55% in the intervention group.

Anemia

A total of 5.9% of the intervention group and 7.6% of the control group had anemia (difference -1.7, CI -4.3 to 0.9) with fewer incidences of anemia in the intervention group. Anemia treated with iron supplements was more common in the intervention group 8.2% versus 3% (difference 5.2, CI 2.9 to 7.6) (Table 9).

Diabetes/dysglycemia

A total of 13% in the intervention group and 9% in the control group had diabetes (difference 3.7 CI 0.5 to 6.8). In the intervention group, preoperative HbA1c in mmol/mol was mean (SD) of 37.8 (7.3) versus 38.1 (7.6) in the control group, (difference -0.2, CI (-1.0 to 0.5)). Regarding non-diabetes mellitus patients, a total of 6.6% of patients in the intervention group and 7% in the control group had dysglycemia with HbA1c 42–47 mmol/mol (difference -0.3, CI -3.3 to 2.6).

Smoking

A total of 3.8% of the intervention group and 7.3% in the control group smoked, (difference -3.6, CI -6.1 to -1.3) (Table 9).

Nutritional status

One (0.1%) patient in the intervention group and one (0.1%) in the control group had albumin < 35 g/L (difference 0.0, CI -0.6 to 0.6), while 2.1% of the intervention group and 16% of the control group had vitamin D < 50 nmol/L preoperatively (difference -14.6, CI -17.6 to -11.7) (Table 8^c). Thus, vitamin D deficiency was more common in the control group.

Comorbidities

Preoperative comorbidities such as hypertension 62% versus 54% (difference 8.0, CI 3.0 to 13.0), heart diseases such as ischemic heart disease 16% versus 11%, (difference 5.2, CI 1.8 to 8.7), arrhythmias 16% in the intervention group versus 14% in the control group (difference 2.1, CI -1.5 to 5.8), and congestive heart failure 4% versus 1.8% (difference 2.3, CI 0.5 to 4.1) were more common in the intervention group compared with the control group. Lung disease was similar in both groups. Renal insufficiency 11% versus 6% (difference 4.9, CI 2.1 to 7.8) was higher in the intervention group, as is the case with preoperative embolism 3.5% in the intervention group versus 0.9% in the control group (difference 2.5, CI 1.1 to 4.2) and deep vein thrombosis 3.6% in the intervention group and 1.4% in the control group (difference 2.3, CI 0.7 to 4.0). Cancer incidence was 13% in the intervention group and 11% in the control group (difference 2.0, CI -1.2 to 5.3).

This higher number of comorbidities resulted in a higher ratio of patients with ASA ≥ 3 in the intervention group, or 32% versus 23% (difference 9.1, CI 4.6–13.6) otherwise, the two groups were similar in age, sex ratios, BMI distribution, operation type, anesthesia, LOS, and laboratory values. Medical complications were uncommon within the first six weeks post-operatively in both groups, and no mortalities were recorded (Table 8).

Table 8. Comparisons of parameters of control and intervention groups 1 week prior to operation, perioperatively and 6 weeks postoperatively. The difference between the 2 groups is calculated between means when presented, otherwise between proportions (shown in brackets) and is presented with 95% confidence interval. Values are count (%) unless otherwise specified.

Patient characteristics 1 week prior to operation	Intervention group (n = 746)	Missing	Control group (n = 738)	Missing	Difference [CI]
Age ^a	67.9 (9.7)		66.7 (8.8)		1.2 [0.3 to 2.2]
Female sex	414 (55)		421 (57)		-1.6 [-6.6 to 3.5]
BMI ^a	31.0 (5.4)		30.6 (5.2)	1 (0.1)	0.4 [CI -0.2 to 0.9]
< 18.5	1 (0.1)		1 (0.1)		0.0 [-0.6 to 0.6]
18.5–24.9	102 (14)		94 (13)		0.9 [-2.5 to 4.4]
25–29.9	231 (31)		258 (35)		-4.0 [-8.8 to 0.7]
30–34.9	241 (32)		238 (32)		0.0 [-4.7 to 4.8]
35–39.9	126 (17)		108 (15)		2.2 [-1.5 to 5.9]
40–44.9	39 (5.2)		33 (4.5)		0.8 [-1.5 to 3.0]
45–49.9	6 (0.8)		5 (0.7)		0.1 [-0.9 to 1.1]
≥ 50	0 (0)		0 (0)		0.0 [-0.5 to 0.5]
Patient comorbidities					
Smoking	28 (3.8)	10 (1.3)	54 (7.3)	11 (1.5)	-3.6 [-6.1 to -1.3]
Hypertension	465 (62)		401 (54)		8.0 [3.0 to 13.0]
Ischemic heart disease	120 (16)		80 (11)		5.2 [1.8 to 8.7]
Arrhythmias	122 (16)		105 (14)		2.1 [-1.5 to 5.8]
Anticoagulation	113 (15)		78 (11)		4.6 [1.2 to 8.0]
Congestive heart failure	30 (4.0)		13 (1.8)		2.3 [0.5 to 4.1]
Lung disease	133 (18)		131 (18)		0.1 [-3.8 to 4.0]
Pulmonary embolism	26 (3.5)		7 (0.9)		2.5 [1.1 to 4.2]
Deep vein thrombosis	27 (3.6)		10 (1.4)		2.3 [0.7 to 4.0]
Diabetes	93 (13)		65 (8.8)		3.7 [0.5 to 6.8]
Renal insufficiency	82 (11)		45 (6.1)		4.9 [2.1 to 7.8]
Transient ischemic attack	42 (5.6)		48 (6.5)		-0.9 [-3.3 to 1.6]
CNS bleeding	4 (0.5)		5 (0.7)		-0.1 [-1.1 to 0.8]
Inflammatory arthritis	51 (6.8)		50 (6.8)		0.1 [-2.5 to 2.7]
Depression	78 (11)		73 (9.9)		0.6 [-2.5 to 3.7]
Anxiety	62 (8.3)		43 (5.8)		2.5 [-0.1 to 5.1]
Cancer	94 (13)		78 (11)		2.0 [-1.2 to 5.3]
Type of operation					
Knee replacement	480 (64)		476 (65)		-0.2 [-5.0 to 4.7]
Hip replacement	266 (36)		262 (36)		0.2 [-4.7 to 5.0]
Type of anesthesia					
Spinal	691 (93)		659 (89)		3.3 [0.4 to 6.3]
General	55 (7.4)		79 (11)		-3.3 [-6.3 to -0.4]
ASA classification					
Class 1	41 (5.5)		44 (6.0)		-0.5 [-2.9 to 1.9]
Class 2	469 (63)		528 (72)		-8.7 [-13.4 to -3.9]
Class 3	236 (32)		164 (22)		9.4 [4.9 to 13.9]
Class 4	0 (0)		2 (0.3)		-0.3 [-1.0 to 0.3]
ASA ≥ 3	236 (32)		166 (23)		9.1 [4.6 to 13.6]
Blood tests					
Haemoglobin, g/L ^a					

Preoperative ^a	140.9 (12.6)		141.3 (13.4)	2 (0.3)	-0.4 [-1.8 to 0.9]
postoperative ^a	112.9 (12.7)	4 (0.5)	115.9 (12.8)	34 (4.6)	-3.0 [-4.4 to -1.7]
postoperative drop ^a	28.0 (8.4)	4 (0.5)	25.8 (10.9)	34 (4.6)	2.2 [1.2 to 3.2]
Anemia preoperative	44 (5.9)	0 (0)	56 (7.6)	2 (0.3)	-1.7 [-4.3 to 0.9]
mild	38 (5.1)		47 (6.3)		-1.3 [-3.7 to 1.1]
moderate	6 (0.8)		8 (1.1)		-0.3 [-1.4 to 0.8]
severe			1 (0.1)		-0.1 [-0.8 to 0.4]
Creatinine, $\mu\text{mol/L}$ ^a					
preoperative	83.9 (47.7)		78.5 (22.6)	2 (0.3)	5.4 [2.5 to 10.7]
postoperative	85.7 (56.0)	5 (0.7)	81.4 (29.3)	34 (4.6)	4.3 [0.6 to 10.3]
Glucose, mmol/L ^a					
preoperative	6.4 (1.5)	1 (0.1)	6.1 (1.5)	13 (1.8)	0.3 [0.1 to 0.4]
postoperative	6.5 (1.2)	12 (1.6)	6.8 (1.3)	38 (5.1)	-0.3 [-0.4 to -0.2]
HbA1c, mmol/L ^a					
preoperative	37.8 (7.3)	7 (0.9)	38.1 (7.6)	17 (2.3)	-0.2 [-1.0 to 0.5]
HbA1c for non-DM patients		7 (1.1)			
42–47 mmol/mol	49 (6.6)		52 (7.0)		-0.3 [-3.3 to 2.6]
> 47 mmol/mol	8 (1.1)		13 (1.8)		-0.7 [-2.2 to 0.7]
Albumin, g/L ^a	43.4 (2.7)	10 (1.3)	44.2 (2.7)	12 (1.6)	-0.7 [-1.0 to -0.5]
Albumin < 35 g/L	1 (0.1)	10 (1.3)	1 (0.1)	12 (1.6)	0.0 [-0.6 to 0.6]
Lymphocytes < $1.5 \times 10^9/\text{L}$	79 (11)	1 (0.1)	129 (18)	2 (0.3)	-6.9 [-10.5 to -3.4]
Vitamin D					
Mean vitamin D, nmol/L ^{a,b}	84.7 (34.5)	5 (0.7)	79.6 (33.9)	16 (2.2)	5.1 [1.6 to 8.7]
Vitamin D < 50 nmol/L ^c	16 (2.1)	20 (2.7)	121 (16)	16 (2.2)	11.7
Peri- and postoperative differences					
Blood transfusions	35 (4.7)		19 (2.6)		2.1 [0.2 to 4.1]
Length of stay (days) ^a	1.9 (3.2)		1.7 (1.7)		0.1 [-0.1 to 0.5]
Postoperative medical complications ≤ 6 weeks from operation					
Myocardial infarction			2 (0.3)		
Heart failure	6 (0.8)		3 (0.4)		0.4 [-0.5 to 1.4]
Pneumonia	3 (0.4)		7 (0.9)		-0.5 [-1.6 to 0.4]
Transient ischemic attack	3 (0.4)		7 (0.9)		-0.5 [-1.6 to 0.4]
Pulmonary embolism	5 (0.7)		3 (0.4)		0.3 [-0.6 to 1.2]
Deep vein thrombosis	3 (0.4)		3 (0.4)		0.0 [-0.8 to 0.8]
Renal insufficiency	24 (3.2)		11 (1.5)		1.7 [0.2 to 3.4]
Death	0 (0.0)		0 (0.0)		0.0 [-0.5 to 0.5]

^a Values are mean (SD)

^b The vitamin D results for the intervention group are based on blood tests taken at decision of operation.

^c Results for number of patients with vitamin D < 50 nmol/L 1 week prior to operation in the intervention group are based on repeated blood tests of those 91 patients that were < 50 nmol/L at decision of operation.

One week preoperatively, patients answered a questionnaire. A higher level of motivation was found in the intervention group with patient's attempting to modify modifiable risk factors compared to the control group. In the intervention group, 70% of patients attempted to lose weight, versus 60% in the control group (difference 10.6, CI (5.8 to 15.4)). In the intervention group 79% of patients increased their movement versus 68% in the control group (difference 11.3, CI 6.9 to 15.8), use of primary health care physical activity in the intervention group did 11% versus 5.7% in the control group (difference 5.4, CI 2.6 to 8.3), physiotherapy used in the intervention group by 36% versus 27% in the control group (difference 9, CI 4.2 to 13.6). Motion incidences/week none in the intervention group 8.8% versus 15% in the control group, where this group of people did not engage in any form of physical activity (difference -6.6, CI -9.9 to -3.3), with 71% in the intervention group attempting to modify their nutrition versus 60% in the control group (difference 11.3, CI 6.5 to 15.8), and smoking at time of surgery in the intervention group 3.8% versus 7.3% in the control group (difference -3.6, CI -6 to -1.2). In the intervention group 93% of patients visited a primary health care physician compared to 7.9% in the control group (difference 85, CI 82 to 88).

The intervention group also had more preoperative visits to other healthcare providers, notably cardiologists 28% compared to 12% in the control group (difference 15.3, CI 11.3 to 19.2) (Table 9).

Table 9. Answers to questionnaire of control and intervention groups at preoperative visit 1 week prior to operation. The difference between the 2 groups is shown with 95% confidence interval. Values are count (%)

Answers	Intervention group			Control group			Difference [CI]
	Yes	Not applicable	Missing	Yes	Not applicable	Missing	
During wait for surgery, have you been informed of following health factors and possible influence of them on the outcome of the operation?							
Weight	613 (82)	35 (4.7)	23 (3.1)	321 (44)	130 (18)	21 (2.8)	38.7 [34.0 to 43.1]
Motion	646 (87)	13 (1.7)	26 (3.5)	381 (52)	112 (15)	18 (2.4)	35.0 [30.5 to 39.2]
Nutrition	591 (79)	19 (2.5)	49 (6.6)	281 (38)	138 (19)	27 (3.7)	41.1 [36.5 to 45.6]
Smoking	355 (48)	276 (37)	48 (6.4)	182 (25)	320 (43)	27 (3.7)	22.9 [18.1 to 27.6]
Anemia	260 (35)	191 (26)	106 (14)	83 (11)	257 (35)	59 (8.0)	23.6 [19.4 to 27.7]
During wait for surgery, have you tried to influence the following health factors?							
Weight	524 (70)	32 (4.3)	38 (5.1)	440 (60)	54 (7.3)	31 (4.2)	10.6 [5.8 to 15.4]
Motion	590 (79)	17 (2.3)	31 (4.2)	500 (68)	45 (6.1)	27 (3.7)	11.3 [6.9 to 15.8]
Use of							
primary care physical activity	83 (11)		482 (65)	42 (5.7)		486 (66)	5.4 [2.6 to 8.3]
physiotherapy	270 (36)		347 (47)	201 (27)		388 (53)	9.0 [4.2 to 13.6]
Motion incidences/week			163 (22)			71 (9.6)	
0	66 (8.8)			114 (15)			-6.6 [-9.9 to -3.3]
1	39 (5.2)			49 (6.6)			-1.4 [-3.9 to 1.0]
2	93 (13)			131 (18)			-5.3 [-8.9 to -1.6]
3	159 (21)			158 (21)			-0.1 [-4.3 to 4.1]
4	115 (15)			93 (13)			2.8 [-0.7 to 6.4]
≥ 5	111 (15)			122 (17)			-1.7 [-5.4 to 2.1]
Motion length, minutes			168 (23)			78 (11)	
0	58 (7.8)			101 (14)			-5.9 [-9.1 to -2.8]
0-20	121 (16)			117 (16)			0.4 [-3.4 to 4.1]
20-40	222 (30)			200 (27)			2.7 [-1.9 to 7.2]
40-60	132 (18)			170 (23)			-5.3 [-9.4 to -1.2]
> 60	45 (6.0)			72 (9.8)			-3.7 [-6.5 to -1.0]
Nutrition	529 (71)	23 (3.1)	52 (7.0)	440 (60)	57 (7.7)	34 (4.6)	11.3 [6.5 to 15.8]
Smoking	142 (19)	422 (57)	92 (12)	102 (14)	450 (61)	66 (8.9)	5.2 [1.4 to 9.0]
Still smoking at time of surgery	28 (3.8)		10 (1.3)	54 (7.3)		11 (1.5)	-3.6 [-6.0 to -1.2]

If previous smoker, when did you quit?			427 (57)			434 (59)	
< 6 weeks	16 (2.1)			6 (0.8)			1.3 [0.1 to 2.7]
6 week to < 6 months	13 (1.7)			6 (0.8)			0.9 [-0.3 to 2.2]
6 months to < 1 year	15 (2.0)			6 (0.8)			1.2 [0.0 to 2.6]
≥ 1 year	275 (37)			286 (39)			-1.9 [-6.8 to 3.0]
Anemia treated with iron supplement	61 (8.2)	259 (35)	97 (13)	22 (3.0)	323 (44)	90 (12)	5.2 [2.9 to 7.6]
During wait for surgery, have you been in contact with other health care providers?							
Primary care	695 (93)			58 (7.9)		102 (14)	85.3 [82.3 to 87.7]
Cardiologist	205 (28)			90 (12)	147 (20)	77 (10)	15.3 [11.3 to 19.2]
Pulmonologist	23 (3.1)	153 (21)	217 (29)	25 (3.4)	180 (24)	90 (12)	-0.3 [-2.2 to 1.5]
Endocrinologist	23 (3.1)	167 (22)	222 (30)	14 (1.9)	206 (28)	90 (12)	1.2 [-0.4 to 2.9]
Nephrologist	21 (2.8)	166 (22)	222 (30)	9 (1.2)	207 (28)	93 (13)	1.6 [0.1 to 3.2]

A questionnaire on services provided and satisfaction¹⁴⁴ was administered to the intervention group a week before operation during the preoperative visit. Values are count (%). The first question, appreciation of hospital service, missing 96 (13%), resulted in a substantial number of patients who were very satisfied with hospital services 265 patients (36%) and 100 (13%) were very dissatisfied. The second question, appreciation of primary health care service, missing 355 (48%), resulted in a total of 109 patients (15%) being very satisfied, whereas 30 (4%) were very dissatisfied. The third question, noticed hospital and primary health care cooperation, missing 224 (30%). A total of 146 (20%) of patients did not observe cooperation between the hospital and primary health care services, while 33 (4.4%) were well aware of the cooperation between the hospital and primary health care providers. Wait time for operation had a mean (SD) of 355 (223) days, with the COVID-19 pandemic causing certain delays in operations, possibly contributing to forgetfulness of cooperation, but this is one fifth of the intervention group.

4.3 Epidemiology of superficial SSI and PJI in Control and Intervention Groups

SSI was assessed at six weeks and one year, while PJI was assessed at six weeks and three years' post-surgery and included surgical site complications at six weeks postoperatively

Table 10. Number of patients followed per year after operation.

	Number of patients followed per year after operation (%)				
	1 yr	2 yr	3 yr	4 yr	5 yr
Intervention group: no 746	741 (99)	692 (93)	549 (74)	178 (24)	1 (0,1)
Control group: no 738	735 (99)	731 (99)	723 (98)	684 (93)	262 (36)

Follow up at six weeks following surgery for Control and Intervention Groups for SSI and PJI

A total of 99% of the control group and 95% of the intervention group were followed up with at the orthopedic outpatient clinic for clinical evaluation; remaining patient information was gathered from hospitals, rehabilitation centers if patients have been admitted, and primary health care. During the COVID-19 pandemic, some patients were contacted by phone by the specialist surgeon. Complete follow up information was obtained for all patients.

Complications from the surgical site were lower in the intervention group compared to the control group: 11.3% vs. 15.7% (difference -4.5%, CI -8.0 to -1.0).

Superficial SSIs were also less common in the intervention group at 5.6% compared to the control group at 7.7% (difference -2.1%, CI -4.7 to 0.4).

In the intervention group, all cases of PJI requiring DAIR within six weeks evolved from superficial SSIs, which occurred in 1.5% of patients. Likewise, in the control group, all cases of PJI evolved from superficial SSIs, which occurred in 0.95% of patients (difference 0.5, CI -0.7 to 1.8) (Table 11).

Table 11. Comparison of surgical site complications between control and intervention groups within 6 weeks after operation. The difference of proportions between the 2 groups is shown with 95% confidence interval. *Values are count (%)*

Surgical site complications	Intervention	Missing	Control	Missing	Difference % [CI]
Any surgical site complications	84 (11)	0	116 (16)	3 (0.4)	-4.5 [-8.0 to -1.0]
Superficial SSI	42 (5.6)	0	57 (7.7)	3 (0.4)	-2.1 [-4.7 to 0.4]
Drainage	37 (5.0)	0	58 (7.9)	3 (0.4)	-2.9 [-5.5 to -0.4]
Bleeding	36 (4.8)	0	42 (5.7)	3 (0.4)	-0.9 [-3.2 to 1.4]
Dehiscence	11 (1.5)	0	12 (1.6)	3 (0.4)	-0.2 [-1.5 to 1.2]
Limb hematoma	23 (3.1)	0	13 (1.8)	3 (0.4)	1.3 [-0.3 to 3.0]
Periprosthetic joint infection	11 (1.5)	0	7 (0.9)	3 (0.4)	0.5 [-0.7 to 1.8]

SSI at one year follow up for the control and intervention group

A cutoff was made at one year for analysis of superficial SSI. The median time from operation to the diagnosis of the 58 superficial SSIs in the control group was 18 days (IQR 14–29), range 2–132) and 21 days for the 44 superficial SSIs for the intervention group (IQR 15–33, range 1–60). Superficial SSI was 7.9% in the control group at one year and 5.9% in the intervention group at one year, superficial SSI lower in the intervention group, with Hasard Ratio (HR) 0.67, 95% CI (0.45–1.01), not significant.

A crude comparison of superficial SSI incidence over one year indicated no significant difference between groups (Gray's test, $p = 0.132$). However, when stratified, incidence was highest in control patients with ASA 3–4 (Gray's test $p = 0.002$) and BMI ≥ 30 (Gray's test $p = 0.041$), with significant differences across curves (Fig. 3).

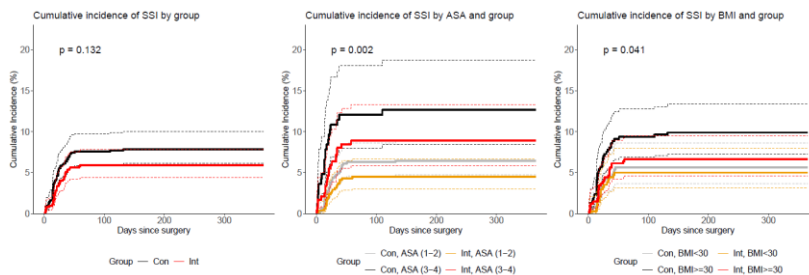


Figure 3. Cumulative incidence of superficial SSI by group, ASA, and BMI categories at 1 year follow up

PJI at three years follow up for the control and intervention group

PJI with follow up till time to event 3-5 years, a cutoff was made at 3 years. The PJI incidence rate was higher in the intervention group (2% versus 1.1% in the control group). A Fine-Gray risk model adjusted for sex, age, and ASA score yielded a higher, though not statistically significant, hazard ratio for PJI in the intervention group: HR 1.80 (95% CI: 0.76–4.30).

A crude analysis showed no significant difference in three-year PJI incidence between groups (Gray's test, $p = 0.142$). Stratified by ASA score, incidence was highest in the intervention group with ASA 3–4, but this was not significant (Gray's test $p = 0.174$). By BMI, incidence was highest in the intervention group with BMI ≥ 30 , showing a significant difference (Gray's test $p = 0.009$) (Fig. 4).

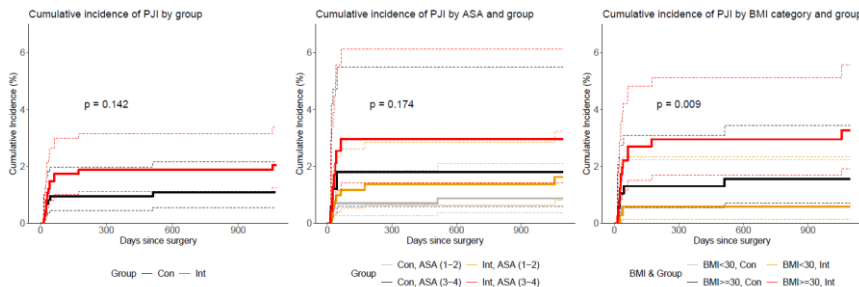


Figure 4. Cumulative incidence of PJI by group and ASA and BMI scores at three years follow up time.

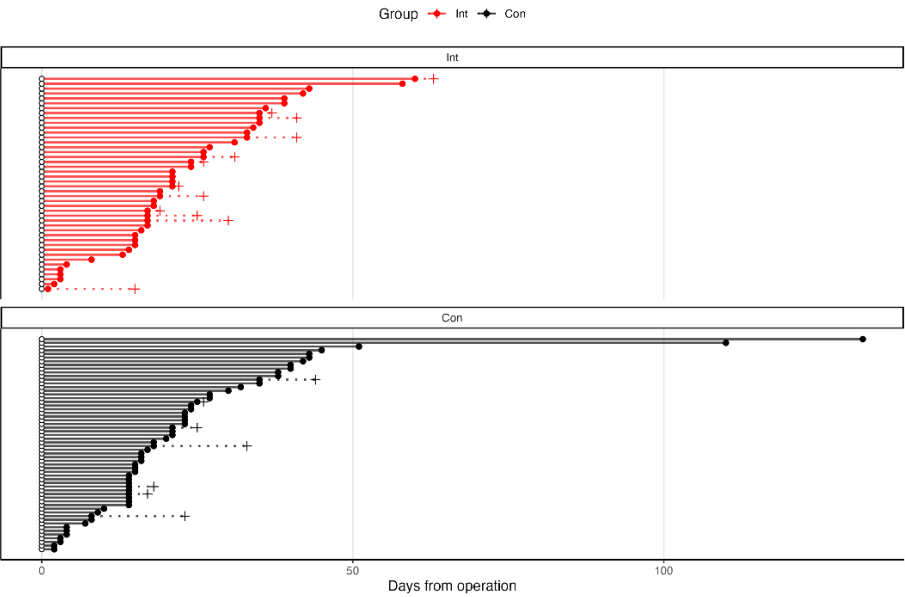
PJI after progression from superficial SSI

The median time from operation to diagnosis for the 15 PJIs in the intervention group was 31 days (IQR 26–52, range 15–1056) and 26 days for the eight in the control group (IQR 22 – 36, range 17–512).

For patients with superficial SSIs that developed into PJIs, the median time between the two diagnoses was six days for the 12 cases in the intervention group (IQR 2–8, range 2–8), and four days for the seven in the control group (IQR 4–12, range 1–15) (Fig 5).

a)

Timeline of SSI patients (with or without subsequent PJI)
Solid lines: time to SSI (●); dotted lines: time to subsequent PJI (+)



b)

Timeline of PJI-only patients (without SSI)
Dotted lines: time to PJI (+)

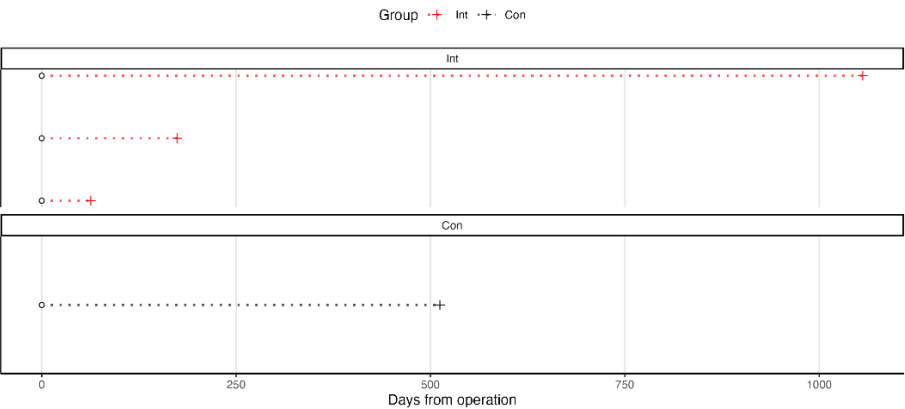


Figure 5. a) Time from surgery to diagnosis of superficial SSI after primary TJA (whole line) and time to diagnosis of PJI after preceding superficial SSI (dotted line). b) Time from surgery to diagnosis of PJI after TJA without preceding superficial SSI.

Seven of eight (88%) PJIs in the control group were preceded by superficial SSIs. In the intervention group, 12 of 15 (80%) PJIs were preceded by superficial SSIs. Of 58 patients with superficial SSIs in the control group, seven progressed to PJIs (12.1%). Of the 44 patients with superficial SSIs in the intervention group, 12 progressed to PJIs (27.3%).

Progression from superficial SSIs to PJIs was more frequent in the intervention group across both ASA categories, with the highest rate (37%) seen in patients with BMI $\geq$ 30 (Table 12).

Table 12. Conversion rate of superficial SSI (SSSI) to PJI according to ASA and BMI score.

	Intervention group 746					Control group 738				
	No (%)	SSSI (6%)	PJI total (2.0%)	PJI without preceding SSSI	PJI generated from SSSI (progression ratio%)	No (%)	SSSI (8%)	PJI total (1.1%)	PJI without preceding SSSI	PJI generating from SSSI (progression ratio%)
ASA 1-2	510 (68)	23 (3)	8 (1.1)	2	6 (27.3)	572 (78)	37 (5)	5 (0.7)	1	4 (10.8)
ASA 3-4	236 (32)	21 (3)	7 (0.9)	1	6 (30.4)	166 (22)	21 (3)	3 (0.4)		3 (14.3)
BMI <30	334 (45)	17 (2)	2 (0.3)		2 (11.8)	354 (48)	20 (3)	2 (0.3)		2 (10.0)
BMI $\geq$ 30	412 (55)	27 (4)	13 (1.7)	3	10 (37.0)	384 (52)	38 (5)	6 (0.8)	1	5 (13.2)

Results are shown as count (%).

In patients that developed superficial SSIs, the mean BMI value was highest in the intervention group ≥ 30 , as was the case in patients that developed PJI (Table 13).

Table 13. Mean BMI values of BMI groups without and with superficial SSI and those that developed PJI. Results are shown as mean BMI (count).

Category (no)								
	Ctrl	Intv	Ctrl no SSI	Intv no SSI	Ctrl SSI	Intv SSI	Ctrl PJI	Intv PJI
BMI <30 (x)	26.3	26.2	26.3 (333)	26.3 (322)	26.6 (20)	26.1 (17)	28.5 (2)	23.9 (2)
BMI ≥ 30 (x)	34.6	34.8	34.6 (346)	34.7 (377)	34.9 (38)	38.0 (30)	34.1 (6)	37.3 (13)

Bacterial cultures during the study time were represented in Table 14 for both SSIs and PJIs during the study period (Table 14).

In this study, among patients with superficial SSIs in the control group, cultures were obtained in 49% of cases, with *Staphylococcus* species identified as the pathogen in 95% and *Pseudomonas* in 5%. In the intervention group, cultures were taken in 48% of superficial SSIs, with *Staphylococcus* species accounting for 86% of identified pathogens; *Staphylococcus aureus* was the most common type in both groups. For PJIs using a time frame set by the Orthopedic Clinic of Landspítali University Hospital, within six weeks (early), in both groups *Staphylococci* were the main type, and *Staphylococcus aureus* was the most common. For PJIs from six weeks up to two years (delayed), *Staphylococci* were also the main type, with two cases of *Staphylococcus epidermidis*, one case of *Staphylococcus aureus* and one case of *Streptococcus dysgalactiae* for both groups. After two years (late), the one pathogen was *Streptococcus pneumoniae*, a hematogenic pyogenic arthritis.

In sum, *Staphylococcus aureus* was the most common pathogen in early PJI infections, while *Staphylococcus epidermidis* was the most common pathogen in delayed infections. *Staphylococci* were thus the most common pathogen in both PJI groups within two years.

Table 14. Positive bacterial cultures ≤ 6 weeks and > 6 weeks up to 1 year in superficial SSI and up to 3 years in PJI after primary total joint arthroplasty. Values are count (%)

	Intervention group (n = 746)		Control group (n = 738)	
	$\leq 6w$	$> 6w$	$\leq 6w$	$> 6w$
Superficial SSI	42 (5.6)	2 (0.27)	57 (7.7)	1 (0.14)
Cultures taken	20	1	28	1
Cultures positive	15	1	18	1
Bacteria considered the main cause of infection				
Staphylococci				
<i>S. aureus</i>	9		10	1
<i>S. epidermidis</i>	4		3	
<i>Coagulase negative s.</i>	1		3	
<i>S. caprae</i>			1	
Streptococci				
<i>Str. dysgalactiae</i>		1		
<i>Pseudomonas</i>			1	
<i>Enterococcus faecalis</i>	1			
Additional bacteria that were cultured				
<i>Enterococcus faecalis</i>			1	
<i>Corynebacter</i>			1	
<i>Proteus Mirabilis</i>			1	
<i>Escherisia coli</i>			1	
<i>Streptococcus agalactiae</i>			1	
<i>Enterobacter</i>	1			
No. of patients with multibacterial infection	1		3	
PJI	11 (1.5)	4 (0.54)	7 (0.95)	1 (0.14)
Cultures taken	11	4	7	1
Cultures positive	11	4	7	1

	Bacteria considered the main cause of infection			
Staphylococci				
<i>S. aureus</i>	6	1	3	
<i>S. epidermidis</i>	3	1	1	1
<i>S. caprae</i>			1	
Streptococci				
<i>Str. dysgalactiae</i>	0	1		
<i>Str. pneumoniae</i>	0	1		
<i>Str. agalactiae</i>			1	
<i>Proteus Mirabilis</i>			1	
<i>Acinetobacter B.</i>	1			
<i>Enterococcus Fecalis</i>	1			
	Additional bacteria cultured			
Staphylococci				
<i>S. capitis</i>		1		
<i>S. lugdunensis</i>			1	
<i>S. epidermidis</i>	2		1	
<i>Corynebacterium tuberculos.</i>	1			
<i>Dermabacter hominis</i>			1	
<i>Acinetobacter pittii</i>			1	
<i>Micrococcus luteus</i>	1			
<i>Corynebacterium</i>	1			
<i>Brevibacterium</i>	1			
<i>Aerococcus viridans</i>	1			
<i>Dermabacter</i>	1			
No. of patients with multibacterial infection	3	1	2	

In the control group there was one case of primary PJI more than six weeks post-operation, two stage operation, or 73 weeks post-operation. The cause of the reoperation was pain with suspected cup loosening, and there was no preceding superficial SSI. *Staphylococcus epidermidis* was diagnosed from preoperative aspiration and perioperative tissue samples (Table 14).

In the intervention group, there were four cases of primary PJI diagnosed more than six weeks postoperatively. Of these, two were managed with DAIR, and two underwent two-stage revision procedures. Three of the four cases were associated with surgical site complications, with the exception of one being a case of hematogenous pyogenic arthritis.

The first DAIR case occurred nine weeks postoperatively and involved leg cellulitis that progressed to a knee abscess. The patient had a history of recurrent preoperative cellulitis, and cultures were positive for *Staphylococcus aureus*. The second DAIR was performed 151 weeks postoperatively in a case of hematogenous pyogenic arthritis accompanied by sepsis, with *Streptococcus pneumoniae* isolated in cultures from the joint.

Of the two two-stage revision cases, one involved fistula formation 60 days after surgery, with the related cultures testing positive for *Streptococcus dysgalactiae*. The other developed cellulitis at the surgical site 63 days postoperatively cultures revealing *Staphylococcus epidermidis* and *Staphylococcus capitis* (Table 14).

In short, three patients in the intervention group experienced surgical site complications: one developed a knee abscess secondary to recurrent leg cellulitis, another presented with fistula formation, and a third had cellulitis at the surgical site. The fourth patient developed hematogenous pyogenic arthritis. Within two years excluding the first six weeks postoperatively there were two cases of *Staphylococci* and one case of *Streptococcus*, and after two years there was one case of *Streptococcus*. Notably, all four patients underwent TJA during the COVID-19 pandemic.

4.4 Association between preoperative modifiable risk factors and development of superficial SSI

The association between preoperative MRFs and postoperative superficial SSI was investigated in the control group at six weeks. An exploratory secondary analysis examined the link between preoperative MRFs and postoperative superficial SSI. The results showed significantly higher odds of superficial SSI in patients with a BMI ≥ 30 (OR 2.1, 95% CI 1.2–3.8) and HbA1c ≥ 42 mmol/mol (OR 2.2, 95% CI 1.1–4.2). No significant associations were found for other risk factors (Table 15).

Table 15. Odds ratio (OR) and (95% confidence interval) of superficial SSI for patients with preoperative risk factors

Superficial SSI	OR (95% CI)	Missing
Preoperative Anemia	0.91 (0.27-2.32)	2
HbA1c ≥ 42 mmol/mol	2.2 (1.1-4.2)	17
BMI at operation ≥ 30 kg/m ²	2.1 (1.2-3.8)	1
Smoking	1.2 (0.41-3)	11
Vitamin D ≤ 50 nmol/L	0.85 (0.38-1.7)	16
Weekly Motion ≤ 2 /week	1.4 (0.73-2.6)	71

The association of preoperative MRFs with postoperative superficial SSI in the intervention group was also investigated at six weeks postoperatively. Patients in the intervention group had undergone preoperative optimization targeting MRFs. However, univariable logistic regression analysis revealed no significant association between superficial SSI and any of the known preoperative risk factors of anemia, HbA1c > 42 mmol/mol, BMI ≥ 30, smoking, vitamin D < 50 nmol/L, or limited physical activity (less than twice weekly), as measured one week before surgery (Table 16).

Table 16. Odds ratio (OR) and 95% confidence interval (CI) of superficial surgical site infections (SSI) for patients in the intervention group with preoperative risk factors 1 week prior to operation

Risk factor	OR (CI)	Missing
Preoperative anemia	0.79 (0.18–3.37)	0
HbA1c ≥ 42 mmol/mol	1.13 (0.51–2.51)	7
BMI at operation ≥ 30	1.20 (0.64–2.27)	0
Smoking	2.12 (0.61–7.32)	10
Vitamin D < 50 nmol/L	2.53 (0.55–11.52)	20
Weekly motion ≤ 2	1.52 (0.72–3.20)	163

Univariable logistic regression analysis revealed no link between superficial SSI at one year and known preoperative risk factors in the intervention group. However, in the control group, elevated BMI (≥ 30) and HbA1c (≥ 42 mmol/mol) were significantly associated with an increased risk of superficial SSI (Table 17).

Table 17. Odds Ratios for Risk Factors Associated with Superficial Surgical Site Infection (SSI). (OR = Odds Ratio; CI = Confidence Interval. Missing data displayed as count/total (percentage)).

	Intervention group		Control group	
	OR (95% CI)	Missing data	OR (95% CI)	Missing data
BMI at operation ≥ 30	1.31 (0.70–2.44)	0/746 (0.0%)	1.83 (1.04–3.21)	1/738 (0.1%)
HbA1c ≥ 42 mmol/mol	1.06 (0.48–2.35)	7/746 (0.9%)	2.09 (1.11–3.91)	17/738 (2.3%)
Preoperative anemia	0.75 (0.18–3.20)	0/746 (0.0%)	0.89 (0.31–2.56)	2/738 (0.3%)
Vitamin D < 50 nmol/L	1.14 (0.47–2.77)	5/746 (0.7%)	0.93 (0.44–1.94)	16/738 (2.2%)
Smoking	2.00 (0.58–6.92)	10/746 (1.3%)	1.19 (0.46–3.12)	11/738 (1.5%)
Weekly motion ≤ 2	0.61 (0.29–1.26)	163/746 (21.8%)	0.92 (0.52–1.64)	71/738 (9.6%)

4.5 Multivariable assessment of the association between intervention group and superficial SSI

In a multivariable logistic regression analysis adjusted for ASA ≥ 3 classification, age, and sex, patients in the intervention group had significantly lower odds of developing superficial SSI compared to those in the control group (OR 0.64, 95% CI 0.42–0.97) (Table 18).

Table 18. Adjusted and Crude odds ratio (OR) and 95% confidence interval (CI) of occurrence of superficial surgical site infections in all patients according to preoperative risk factors 1 week prior to operation. 3 observations were deleted due to missingness. Adjustments were made for ASA class $\geq$ III, age, and sex.

Risk factor	Adjusted OR (95% CI)	Crude OR (95% CI)
Group: Intervention	0.64 (0.42–0.97)	0.71 (0.40–1.07)
ASA class III or above	1.83 (1.17–2.82)	
Age	1.02 (0.99–1.04)	
Male sex	1.67 (1.11–2.54)	

4.6 Long term effects on postoperative general health

Patients in the intervention group had higher incidences of comorbidities and events preoperatively but lower postoperatively (Fig 6); this led to higher ASA scores in the intervention group (Table 8). A negative binomial regression analysis, adjusted for age, sex, and ASA classification and accounting for differences in follow up time, showed no statistically significant difference in the incidence of health-related diagnoses (IRR 0.79; 95% CI: 0.61–1.02) or health-related events (IRR 0.94; 95% CI: 0.59–1.49).

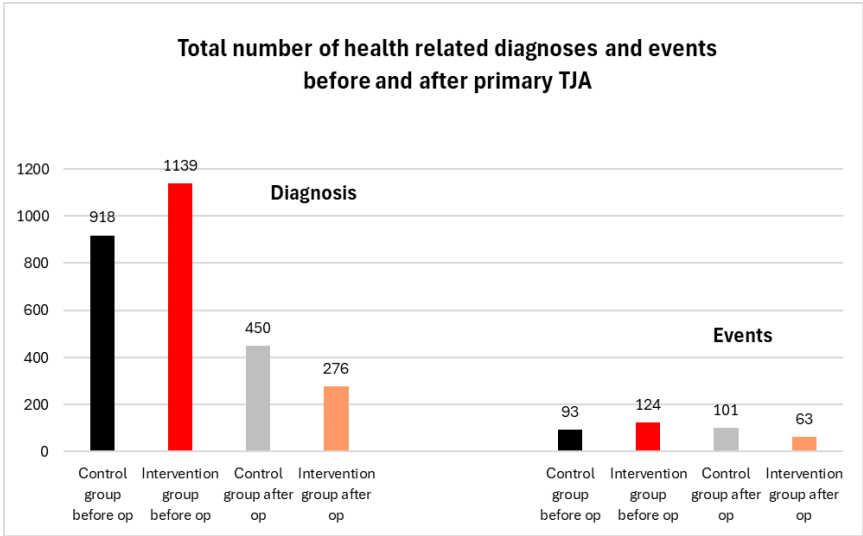


Figure 6. All health-related diagnoses and events before and after operation

Analysis of the cumulative incidence of the first health-related diagnosis postoperatively revealed no significant difference between groups, though the intervention group had a slightly lower incidence (16.6% vs. 20.5%, Gray's test $p = 0.078$). Likewise, no significant difference was observed for new health-related events (5.1% vs. 5.3%, Gray's test $p = 0.897$) (Figure 7).

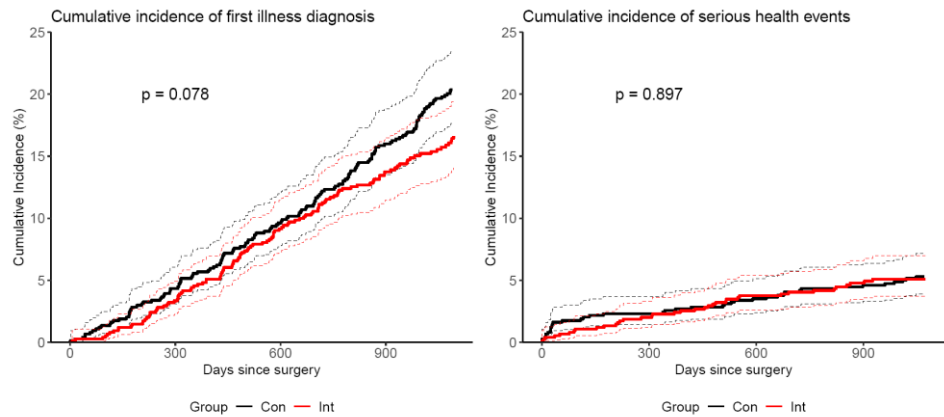


Figure 7. Cumulative incidence of the first health-related diagnosis and events postoperatively

Visits to the emergency department and admissions to the hospital and ICU. The cumulative incidence of the first postoperative visits to the emergency department (46.0% vs. 44.6%), hospital admissions (39.4% vs. 41.6%), and intensive care stays

(4.7% vs. 4.5%) was similar between the intervention and control groups, with no significant differences between the curves at a cutoff of three years (Figure 8).

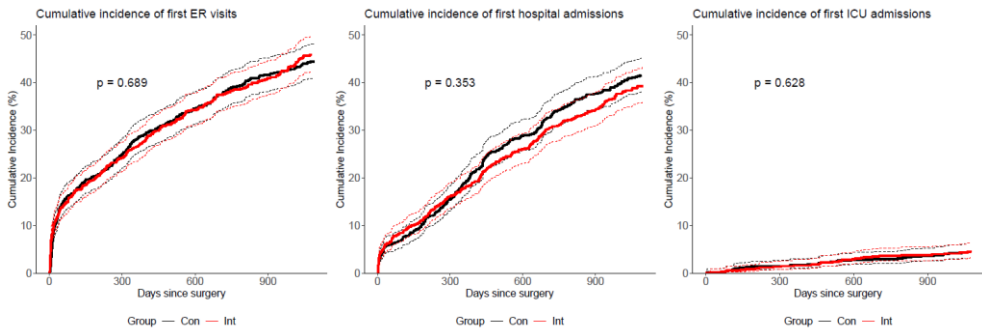


Figure 8. Cumulative incidence of visits to the emergency department and admissions to the hospital and ICU

Mortality rates were similar between groups, with a 98.1% three-year survival rate in the intervention group versus 97.6% in the control group, with no significant difference in survival curves (log-rank test $p = 0.553$). However, when stratified by ASA scores a significant difference in survival curves emerged (log-rank test $p < 0.001$). No significant differences were found when stratified by BMI (log-rank $p = 0.909$) (Figure 9).

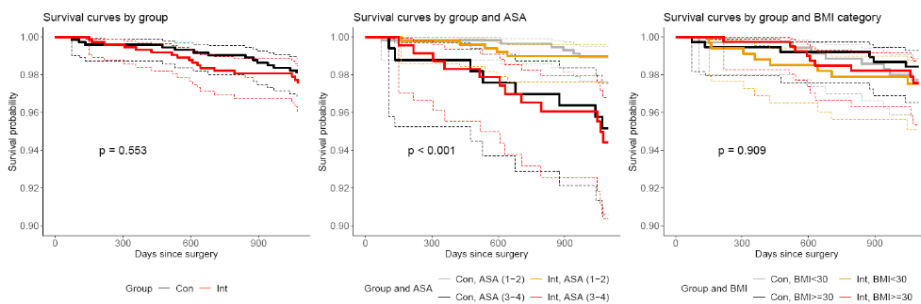


Figure 9. Kaplan-Meier survival curves by treatment group, ASA classification, and BMI category

Flow chart of long-term outcomes after operation for both groups regarding superficial SSI, DAIR operations, two-stage operations, and revision arthroplasties. Revision arthroplasties were more common in the intervention group (3.5% versus 1.9%) (Figure 10).

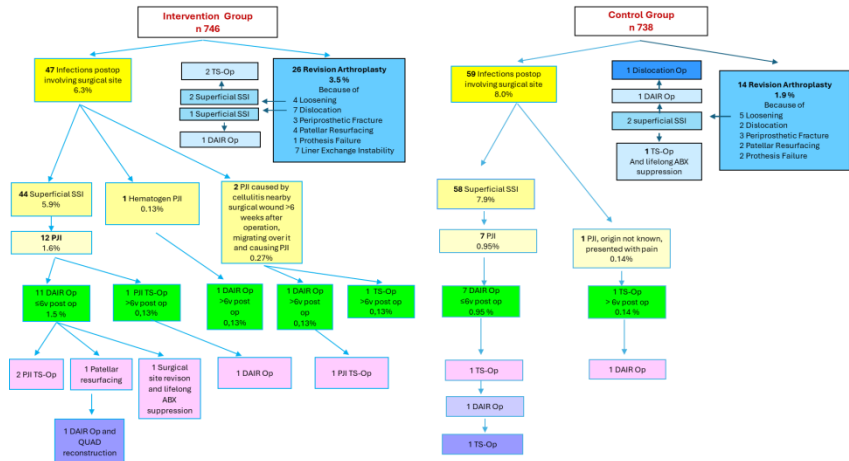


Figure 10. Postoperative infectious complications and revision arthroplasties after primary joint arthroplasty in the intervention and control groups (DAIR Op: debridement, antibiotics and implant retention, TS-Op: two stage operation).

5 Discussion

This prospective case control study conducted at a single institution in cooperation with primary health care indicate that implementing a simple and straightforward optimization strategy increased patient engagement, improved MRFs before operation, decreased short-term superficial SSIs, and reduced surgical complications. However, there was no noticeable effect on the incidence of PJIs after three years or general health.

Control Group: The prevalence of MRFs in an Icelandic cohort undergoing primary TJA after receiving conventional preoperative preparation revealed an association between high BMI and diabetes/dysglycemia and short-term superficial SSI.

Intervention Group: The effect of the optimization pathway involving cooperation between the hospital and primary health care resulted in improvements in weight, anemia, HbA1c, vitamin D, and patient engagement.

Comparison of Intervention and Control Group

In comparison with the control group up to six weeks postoperatively there were fewer superficial SSIs in the intervention group. However, this did not affect the occurrence of PJIs.

According to the three-year follow-up, the intervention produced no effect on the occurrence of PJIs between groups or on long-term general health and mortality.

While this research focused on five key risk factors, it is important to note that many studies typically address only one risk factor at a time, and there is considerable variation in the types of risk factors examined across different studies, complicating comparison ^{144,145}.

There are few existing prospective studies on preoperative optimization that have sought to improve understanding of known risk factors for infectious complications to mitigate them and other complications by comparing control and intervention groups. Studies on preoperative optimization have mostly been performed using databases and retrospective data. These studies have highlighted improved effects of preoperative optimization on SSI ¹⁴⁶, PJI ¹¹², total complication rates ¹⁴⁶, LOS ¹¹¹, post operation visits to emergency wards ¹⁴⁷ and hospital readmissions postoperatively ¹¹³, costs, and patient engagement ¹⁴⁸. This is comparable to the

present study's findings of improvement in patient engagement, early total complication rate, and early superficial SSI rates following MRF optimization ¹⁴⁴.

The key aspect of joint replacement management is SSI prevention ¹¹⁷. Many consider that adherence to preoperative optimization of MRFs, antibiotic prophylaxis, sterile intraoperative techniques, and proper postoperative wound care should be routine to reduce the risk of SSI and thereby enhance patient safety and surgical outcomes ¹⁴⁹.

Increasing emphasis has been placed by health care providers on the preoperative optimization of patients undergoing TJA both to improve individual patient outcomes and to reduce the overall burden on the healthcare system ^{25,150}. Patient selection and methods for optimization are not clear.

5.1 Control group: Prevalence of modifiable risk factors in an Icelandic cohort undergoing TJA. Paper I

The patients in the control group received conventional preoperative preparation before TJA, with preoperative evaluations and blood tests taken one week before surgery.

Knee surgeries accounted for two thirds of all TJAs, with 89% performed under neuraxial anesthesia, in line with recommended practice ¹⁵¹.

Patient characteristics were comparable with other studies (Table 8) ¹⁵²⁻¹⁵⁴, enabling reasonable comparison.

Preoperative anemia was present in 8% of patients, in contrast to 15% to 30%, as reported in other studies ⁵⁸.

Diabetes was present in 9% of patients, as compared to 6% to 12% in other countries ¹⁵⁵. Among non-diabetic individuals, 8% had dysglycemia and 2% had previously undiagnosed diabetes. In comparison, the prevalence of undiagnosed diabetes in similar populations has been reported to be as high as 41% ¹⁵⁶.

At the time of surgical decision-making, 44% of patients self-reported a BMI ≥ 30 , which increased to 52% (Table 8) at the time of surgery based on measured values ¹⁵⁴. Clinical guidelines support weight loss to reduce the risk of periprosthetic joint infection, though no consensus exists on the optimal method for achieving such weight loss.^{157,158} The distribution of BMI categories in this study was comparable to that reported in a recent U.S. study ¹⁵⁹.

Estimated nutritional status was quite good, with only one patient with albumin below 35 g/L. Vitamin D deficiency occurred in 16% of patients (Table 8), as compared to 42% in the United States, ranging from 13% to 80%⁸⁵.

Regarding smoking, 7% of patients reported smoking, with 3% stopping within a year of operation (Table 9).

Patients reported no exercise or motion in 15% of cases, and use of physiotherapy and prescribed physical activity by primary health care with digital follow up was low (Table 9)¹⁴¹. Thus, there is more room to improve patients' physical status³⁰.

Superficial SSIs at six weeks were observed in 8% of cases (Table 11); this is higher than the 1% to 2.5% reported in the United States¹²², but comparable to the 7% reported in Sweden⁹.

Based on the findings, the rates of several MRFs associated with superficial SSI were in the lower range compared with previous studies. However, the rate of superficial SSI was higher. In addition, an association was found between high BMI and diabetes/dysglycemia and short-term superficial SSI.

5.2 Effect of an optimization pathway on modifiable risk factors and short term outcomes. Paper II

5.2.1 Effect of optimization effort on Intervention group from decision of operation until one week before operation (Table 7)

The results of preoperative optimization on MRFs after a straightforward optimization intervention reflected improvements in the MRFs (Table 7), with 93% of patients attending primary health care facilities after the operation decision was made (Table 9). The intervention group patients exhibited more awareness and motivation to optimize MRFs while awaiting surgery compared to the control group (Table 9).

BMI among intervention group patients decreased, with the most marked effect in patients with BMI ≥ 40 kg/m², the number of patients reduced from 8.4% to 6% (difference -2.4%, CI -3.9 to -1.0). In addition, vitamin D deficiency decreased for those who were under 50 nmol/L at the time of the operation decision, with the mean value (SD) increasing from 36.2 (9.3) to 70.9 (28) (difference 34.7, CI (28.6 to 41.5), one week before surgery. Patients with BMI ≥ 40 kg/m² and D vitamin deficiency < 50 nmol/L received hospital-based clinical nutritionist consultations. Patients with anemia also decreased from 7.4% to 5.9% (difference -1.5, CI -3.4 to 0.4); 8% of patients were treated with iron supplements preoperatively.

Diabetes showed better control, with lower long-term HbA1c values one week before operation, mean (SD) 37.8 (7.3), than at the time of the operation decision, mean (SD) 38.2 (7.6) (difference -0.4 , CI -0.7 to -0.1).

5.2.2 Comparison of intervention and control group a week before operation (Table 8)

Age in the intervention group mean (SD) 67.9 (9.7) and the control group 66.7 (8.8) (difference 1.2, CI (0.3 to 2.2). The intervention group was one year older on average and waited longer to undergo operation due to the COVID-19 pandemic.

However, age and sex distribution were similar, as was BMI distribution, and other factors such as type of operation, anesthesia, LOS, and laboratory values were also comparable.

Several differences also emerged between the groups. In particular, preoperative comorbidities like hypertension, ischemic heart disease, and congestive heart failure were more common in the intervention group preoperatively, as were arrhythmias, diabetes, and renal insufficiency. As a result, there was a higher ratio of patients with ASA ≥ 3 classification in the intervention group 32% versus 23% (difference 9.1%, CI 4.6–13.6).

Age is considered to have an effect on surgical outcomes. Older patients are at increased risk for postoperative complications, admission to the ICU, discharge to a skilled care facility, and longer hospital LOS. Rates of complications increased progressively with increasing age¹⁶⁰. There were no mortalities within six weeks, and postoperative medical complications were also low.

In the control group, the incidence of anemia was 8%; 3% of patients received iron treatment, and 3% received blood transfusions. In the intervention group, anemia incidence was 6%; 8% of patients received iron treatment, and 5% received blood transfusions (difference 2.1, CI 0.2 to 4.1). Arrhythmia incidence was higher in the intervention group 15% versus 11% (difference 4.6, CI 1.2 to 8.0), possibly causing higher use of anticoagulants in the intervention group. Increased transfusion rates in the intervention group may have been caused by increased use of anticoagulants, and increased anemia treatment in the intervention group may have decreased the number of blood transfusions needed (Table 8).

Blood loss and allogenic transfusions have been associated with an increased risk of SSIs and PJIs in primary TJA¹⁶¹. Parvizi et al. demonstrated that the use of intravenous (IV) tranexamic acid perioperatively could reduce the incidence of PJI in primary TJA, likely by decreasing blood loss. This results in fewer allogenic blood transfusions, reducing concerns about the immunomodulatory effects of transfusions

¹⁶². Tranexamic acid has also been shown to decrease the occurrence of PJI after aseptic revision arthroplasty, but preoperative anemia has been identified as an independent risk factor for PJI ¹⁶³.

5.2.3 Effect on short term postoperative complications and health

The incidence of early superficial SSI at six weeks following TJA was 8% in the control group and 6% in the intervention group. These rates are consistent with those in other Nordic countries, such as Sweden, which reports a 7% rate of superficial SSI ⁹. However, these rates are higher than those typically reported in the United States, which range from 1% to 2.5% ¹²².

No significant association emerged between known MRFs and superficial SSI in the intervention group (Table 16), whereas elevated BMI ≥ 30 and HbA1c ≥ 42 mmol/mol were linked to increased SSI risk in the control group (Table 15).

This suggests that preoperative optimization may have mitigated these risks. Despite a higher burden of comorbidity, the intervention group had significantly lower odds of developing superficial SSI, likely reflecting the benefits of a multidisciplinary optimization approach ¹¹⁰.

No significant difference in PJI rates (1.5% in the intervention group and 0.9% in the control group) was observed between groups, though the study was not powered for this outcome. These rates are consistent with prior studies ^{9,146,164}.

All cases of PJI within six weeks developed from superficial SSI with progression rate of 12.3% (7/57) of cases in the control group and 26.2% (11/42) in the intervention group, both of which are below the 29% progression rate reported in Sweden ⁹. These figures fall within the reported PJI range of 0.5%–2.5% found in other studies and are comparable to the 1.45% rate reported by the Swedish Knee Arthroplasty Register ^{10,123}.

All superficial SSIs that progressed to PJI were treated with DAIR within six weeks.

Surgical site complications in the control group at six weeks were higher than in previous reports 16% compared with 5.5%–14.3%, though the definition of complications may vary across ¹⁶⁵. However, complications were comparatively lower in the intervention group, 11% (difference -2.1 , CI $(-8 \text{ to } -1)$) (Table 11).

Despite the intervention group having a higher baseline prevalence of comorbidities (see Table 8), they benefited from preoperative optimization (Table 7). After adjusting for confounding variables such as ASA class $\geq$ III, age,

and male sex, the intervention group demonstrated a lower incidence of superficial SSI (Table 18).

5.3 Effect on long-term postoperative complications and health (Paper III)

The follow up time range of the occurrence of superficial SSI varies, from 30 days to 6 months postoperatively ^{166,167}. This study implemented a one-year follow-up, with the latest SSI case diagnosed at 132 days, though the majority were identified within 30 days, 95% in the intervention group and 98% in the control group ¹⁴⁵.

Reported SSI rates after TJA range from 1%–10% ⁹, coinciding with our findings of 5.9% in the intervention group and 7.9% in the control group. The difference was significant at six weeks (Table 18) and also approached significance at one year. A Fine-Gray risk model adjusted for ASA, age, and gender testing for superficial SSI in the intervention group, showed a lower but not significant hazard ratio of 0.67 (95% CI 0.45–1.01) ¹⁴⁵.

Based on the cumulative incidence analysis, ASA score was more associated than BMI with the occurrence of superficial SSI (Fig 3). No preoperative risk factors were associated with SSI in the intervention group, while elevated BMI (≥ 30) and HbA1c (≥ 42 mmol/mol) were significant in the control group, mirroring earlier findings (Table 17). This may suggest that the intervention reduced the impact of these risk factors despite higher disease burden in the intervention group.

Periprosthetic Joint Infection (PJI).

Within three years, in the intervention group PJI incidence was 2% while the control group's incidence was 1.1%, consistent with previously reported rates ^{2,145,168}. In the intervention group, 80% of PJI was preceded by superficial SSI, as compared to 88% in the control group. PJI usually developed within a week, with the infection risk at its highest within 30 days from surgery ¹⁴⁵.

In the intervention group, superficial SSI progressed to PJI in 27.3% of cases, as compared to 12% of control group cases. Eriksson reported a 29% progression rate, similar to the intervention group in this study ⁹. In the intervention group, patients with BMI ≥ 30 showed the highest progression rate (37%) (Table 12).

The cumulative incidence indicated that BMI is more associated with PJI than ASA score, in contrast to a recent study by Wall (2025) showing the opposite ¹⁶⁹. Interestingly, while superficial SSI was less common in the intervention group, PJI

was more frequent. The factors driving progression from superficial SSI to PJI remain unclear but likely involve both patient-related factors and microbial virulence^{170,171}. Additionally, PJI without preceding superficial SSI was more frequently observed in the intervention group¹⁴⁵.

Near the end of the control study period, the orthopedic clinic introduced a change in follow up for suture removal in the control group. Patients with knee prostheses were referred to the hospital's preoperative clinic for suture removal at 2–3 weeks post-operation, while hip prosthesis patients continued to have suture removal managed in primary health care. This shift was motivated by concerns over a potentially higher infection risk in knee prostheses. Superficial SSIs were diagnosed by both primary healthcare providers and the hospital according to the CDC definition of infections, and symptoms were recorded in patients' journals. These notes were confirmed during registration in this studies database, minimizing risk for differences in diagnosis between groups.

However, the impact of this change on the follow-up and detection of surgical site complications remains uncertain. The intervention group had a higher incidence of comorbidities and ASA classification and therefore may have been at risk for increased complication rate, and one wonders what the results would have been without preoperative optimization as PJI rates were not significantly higher compared with the control group.

Effect on Postoperative General Health

Preoperative optimization decreased superficial SSI and surgical site complication rates and increased patient engagement, supporting past findings^{112,144,146,148}. Decreased LOS^{111,147}, and readmissions¹¹³ also occurred. However, the results did not confirm long-term general improvement on general health¹⁴⁵.

Health-related long-term diagnosis or comorbidities and acute events before operation showed increased incidence of comorbidities in the intervention group, as well as increased incidence of health-related acute events. Post-operative follow up with a cutoff at three years revealed a decrease in health-related long-term diagnosis and a decrease in health-related acute events, without significance.

Incidence rate ratios (IRRs), adjusted for sex, age, and ASA classification and accounting for variable follow up time, indicated no significant difference for health-related long-term diagnosis (IRR 0.79; 95% CI 0.61–1.02) nor for health-related acute events (IRR 0.94; 95% CI 0.59–1.49).

Cancer diagnosis might have affected outcomes in health-related long-term diagnosis, though cumulative incidence of first illness diagnosis was nonsignificant for either group (Fig 7).

Despite this shift from higher rates of long-term and acute health events, cumulative rates of new long-term diagnoses, and acute health events (Fig 7), emergency department visits, hospital admissions, and ICU stays were similar across groups (Fig 8). Mortality rates were also comparable (Fig 9). However, mortality was significantly higher among ASA 3–4 patients, regardless of group; no such trend was observed for BMI, supporting findings that ASA is more predictive of mortality than BMI (Fig 9) ¹⁷².

5.4 Preoperative optimization

The aim of preoperative optimization is to reduce postoperative complications—particularly infections, which significantly diminish patients' quality of life and impose substantial healthcare costs ^{173,174}. This is reflected in the increasing focus on preoperative optimization of MRFs driven by health care providers and by bundle care payment models ¹⁷⁵.

However the structure of preoperative optimization programs varies widely; some are hospital-centered, others led by primary health care, and some involve coordinated efforts between both sectors ¹¹¹⁻¹¹³. There is also considerable variation in which risk factors are targeted and the thresholds set for optimization ¹⁰⁹.

Primary health care as the center of preoperative optimization before TJA as primary health care providers often have long-term relationships with patients and offer continuity and follow-through.

Osteoarthritis is a chronic disease that, like many other MRFs, may already be under primary health care management ensure continuous treatment before and after surgery.

There is no formal preoperative optimization clinic attached to hospitals in Iceland, and hospital resources are often scarce, specialist-dependent, and costly. Primary health care is typically more accessible, provides a more holistic approach, and may offer lower costs. However, primary health care resources may also be scarce, and the approach used may have been too weak to induce a real change in patients' care or lifestyle. A checklist should have been included for each patient visiting primary health care for follow up of the five modifiable risk factors chosen for preoperative optimization. There was a large difference in patients' engagement with and improvement in MRFs.

A study on obesity by Fournier emphasized that primary health care physicians are often the patient's first point of contact for referral to TJA and are also commonly responsible for initiating preoperative weight loss interventions ¹⁷⁶.

Despite increasing attention, relatively little has been published on the design, implementation, and effectiveness of preoperative optimization programs ^{108,177}. A recent literature review of 69 studies on preoperative optimization of MRFs identified only three randomized controlled trials and eight prospective cohort studies. Many of these studies focused on a single factor ¹³, limiting direct comparability with our multifactorial approach.

Nonetheless, the overall body of evidence suggests that preoperative optimization is associated with improvements in superficial SSIs ¹⁴⁶, PJIs, ¹¹², total complication rates ¹⁴⁶, hospital LOS ¹¹¹, postoperative emergency visits ¹⁴⁷, hospital readmissions ¹¹³, healthcare costs, and patient engagement ¹⁴⁸, although the magnitude of these benefits varies. These findings are somewhat consistent with our study, which demonstrated that preoperative optimization enhanced patient engagement as well as reduced both total surgical complication rates and short-term superficial SSIs, highlighting the value of cooperation between hospitals and primary health care services, may be a stimulus to future preoperative optimization in a similar manner ¹⁴⁴.

Patients who underwent knee prosthesis in the intervention group were followed up at the hospital's outpatient clinic for suture removal, which may have sharpened and reduced the number of superficial SSI diagnoses and surgical site complication diagnoses and encouraged earlier treatment. The journal records did not indicate overdiagnosis of superficial SSI in the control group.

The intervention group had higher ASA scores, and without preoperative optimization it is impossible to know what the results would have been. Patients are never as motivated to engage in lifestyle changes as before operation, and this is important to preserve during this period ¹⁷⁸. Intervention patients visited primary health care centers in 93% of cases, up from 8% in the control group; thus, patients seemed to be motivated for optimization before surgery, which supports this as a future pathway.

Cooperation between the hospital and primary health care was supported by patient referral between the two institutions. After patients visited the orthopedic outpatient clinic, the hospital booked an appointment at the primary health care within two to three weeks. Though this proved to be a cumbersome step, it needs to be considered in future decisions for pathway implementation on preoperative

optimization, including how best to secure a patient's visit to primary health care, such as by using electronic communication technology.

Following the project, orthopedic surgeons now encourage patients to visit primary health care. Future plans for implementation of structured preoperative optimization pathways should be encouraged to support patient outcomes.

5.5 Methodological considerations

5.5.1 Superficial Surgical Site Infection (SSI) as primary outcome

Superficial SSI was selected as the primary outcome to increase statistical power due to the limited sample size. While this choice may be debated, it is supported by the fact that superficial SSI preceded most cases of PJI. Prior studies have demonstrated a high risk of progression from superficial SSI to PJI in TJA, with one Swedish study reporting a 29% progression rate ⁹. Risk factors for developing superficial SSI, and consequently PJI, include BMI ≥ 30 , HbA1c ≥ 42 , and ASA classification ≥ 3 ^{9,49}.

SSI has been shown to increase the risk of developing PJI by up to 35 times ^{8,9}. In this study, all 11 cases of PJI in the intervention group developed from superficial SSI within six weeks and were treated with DAIR. The virulence of infecting organisms is also a key factor in the progression from SSI to PJI, along with patient-specific risk factors ^{171,179}.

Staphylococcus aureus is often the most common cause of SSI in patients undergoing hip and knee arthroplasty, including up to 20% MRSA ⁴¹. MRSA was not identified in the Icelandic TJA cohort of this study (Table 14).

Comparable results in control and intervention groups were superficial SSI caused firstly by *Staphylococcus aureus* and secondly by *Staphylococcus epidermidis* (coagulase-negative *Staphylococcus*). Similarly, DAIR infections ≤ 6 weeks in both groups were caused firstly by *Staphylococcus aureus* and then by *Staphylococcus epidermidis* (Table 14).

Giuseppe Longo et al. explored the success rate of DAIR treatments in their cohort with early postoperative or acute hematogenous PJI, ranging from 55.5% up to a maximum of 90% (mean value of 71%). The most common pathogen involved was *Staphylococcus aureus*, present in nine out of 12 studies, as was the case in this project's control and interventional groups ^{133,144}. This study's findings were higher than the mean 71% DAIR success rate reported by Longo for both the control and intervention groups. In this study, DAIR operations were performed for acute joint infections ≤ 6 weeks. Success rates for DAIR in these cohorts ≤ 6 weeks were 86%

for the control group and 82% for the intervention group. One acute hematogenous PJI after 151 w was treated with DAIR in the intervention group increasing success rate to 83%.

DAIR operations seem to be a valid choice of first treatment for early joint infections and acute hematogenous PJI operations ^{133,145}.

The incidence of PJI is projected to increase significantly by 2030, with a predicted rate of 6.8% for knee arthroplasty and 6.5% for hip arthroplasty, reflecting the growing burden of PJI as the demand for TJA continues to rise ¹⁸⁰. Currently, PJI is the primary indication for revision arthroplasty ³². Prevention of superficial SSI and PJI is considered more important than the diagnosis and treatment of these conditions. Given the multifactorial nature of infection risk, it is crucial that all healthcare professionals work together to implement a range of prevention strategies ¹⁴.

The success of TJA is heavily dependent on avoiding early postoperative wound complications. If wound drainage develops, it can progress to full-thickness soft tissue necrosis, which, if not addressed promptly, can lead to PJI. Therefore, MRFs should be addressed preoperatively, and perioperative surgical techniques and algorithms should be employed to manage persistent wound drainage effectively ¹¹⁶.

5.5.2 Effects of the COVID-19 pandemic

During the study period, the COVID-19 pandemic caused disruptions and delays. While only 5% of patients in the control group underwent surgery during the pandemic, 77% of the intervention group did. During the pandemic, health care systems experienced disruptions affecting staffing, surgical prioritization, and preoperative and postoperative practices, with social restrictions possibly influencing the quality of follow up, which may have potentially affected outcomes.

An international longitudinal cohort study by 18 countries in 2020 indicated that UK operating theatre capacity decreased by a mean of 63.6%, with a concomitant 27.3% reduction in surgical staffing ¹⁸¹. Increased susceptibility to infections in the initial post-COVID-19 years have been reported, especially to respiratory viruses but also to invasive infections of streptococcus group A and other bacterial coinfections ^{182,183}, which was also noted in Iceland ¹⁸⁴. 44

There are conflicting reports regarding the impact of the COVID-19 pandemic on complications following TJA. Some studies noted a decline in SSIs during the pandemic, such as Karlsen et al.'s ¹⁸⁵ work on Norway. In contrast, other studies report no significant change in SSI rates, including findings from Mimura et al. ¹⁸⁶ in Japan and Humphrey et al ¹⁸⁷. Meanwhile, Plummer et al. ¹⁸⁸ observed a general

increase in SSI during the pandemic, and Momtaz et al.¹⁸⁹ reported higher complication rates after orthopedic surgery. Additionally, Heckman et al.¹⁹⁰ determined that patients who contracted COVID-19 shortly after primary TJA experienced increased complication rates and mortality.

A study by Forlenza during the pandemic highlighted complications in TJI operations within 90 days after patients contracted the virus. COVID-19 diagnosis was associated with increased odds of deep vein thrombosis (OR 4.86, 95% CI 2.10–11.81, $P < .001$); pulmonary embolism (OR 6.27, 95% CI 2.57–16.71, $P < .001$); and complications (OR 3.36, 95% CI 2.47–4.59, $P < .001$) such as cardiopulmonary complications, thromboembolic disease, renal injury, and urinary tract infections. Incidence of deep vein thrombosis/pulmonary embolism was greater the closer in time the COVID-19 diagnosis was to the surgical procedure (10.24 times at 1 month, 7.87 times at 2 months, and 1.42 times at 3 months; $P < .001$). All complications had a similar relationship¹⁹¹.

5.5.3 Effect of private operating clinics and other hospitals

In 2017, Klinikin became the first private clinic in Iceland to offer hip and knee arthroplasties patients could pay for out of pocket. During the period of this research, elective surgery was minimal due to the COVID-19 pandemic. As such, the waiting lists for TJA grew even longer. Midway between 2021, the minister of health decided to begin a yearlong effort to increase the capacity for TJA operations. Other hospitals were engaged in the project, and some patients chose private clinics for their operations. In March 2023, the Government of Iceland decided to fund these operations with taxes¹⁹². Patients gained access to private clinics after being on the waiting list in the public sector for three months.

Patients undergoing surgery in private clinics are most likely those classified as ASA I–II, with some stable ASA III patients possibly included. As a result, patients with ASA III or higher classifications are more likely sent to hospitals, where preoperative optimization will be more critical than ever. Revision arthroplasties, including procedures to address joint infections, are expected to comprise a significant proportion of hospital cases. The Government of Iceland (Stjórnarráð Íslands) has begun a project on the central research platform for infrastructure (Miðlægur rannsóknaveitvangur fyrir innviði)¹⁹³. The Directorate of Health in Iceland has established a central waiting list for surgeries, including TJA, with an interactive dashboard for public information¹⁹⁴. Patients are referred by public hospitals to the central waiting list when an orthopedic surgeon's decision to operate has been made. Preoperative optimization does not take place by this time. The waiting time for hip or knee operation may range from four to 36 weeks (wait times are shorter in

the private sector) ¹⁹⁴. This could improve services for patients awaiting hip or knee TJA. It also supports centralized preoperative optimization by primary health care as patients wait to learn what their surgery decisions are, and which operating clinic or hospital will perform the surgery.

5.5.4 Strengths and limitations

The strengths of the study include its prospective gathering of data, detailed data collection, with follow up window from one to five years (with a cutoff at one year for superficial SSIs and at three years for PJI), and minimal missing clinical data. No selection due to health status was made. The demographics of the study groups are similar to those of other studies, allowing comparability.

The limitations of the study include the low number of patients examined. Additionally, the COVID-19 pandemic slowed the execution of the study, with a possible loss of patients that may have caused unknown effects on the results. In the control group, patients were enrolled just one week before surgery, thus requiring minimal patient involvement. In contrast, the intervention group was recruited 6–12 months in advance and received more interaction with the healthcare system, likely demanding greater patient commitment. This may have led to increased participation by individuals with known health conditions. Additionally, heightened awareness and concern about superficial SSI among both patients and physicians in the intervention group may have contributed to a higher rate of reported diagnoses.

5.6 Future perspectives

Osteoarthritis impacts more than 500 million around the globe ¹. In Iceland, it is predicted that hip TJA (including bipolar prosthesis for hip fractures) will grow from 800 per year in 2019 to 1,500 year 2050, and knee TJA will reach 1,350 operations per year by 2050, or about a 50% increase from 2019 ¹⁹⁵. It is therefore of high importance to decrease the risk of surgical complications after TJA.

A deeper understanding of quality of care requires measuring what matters to people in patient-reported outcomes for TJA. In all OECD countries, TJA results in an improved average quality of life 6–12 months following hip surgery, reaching a score ≥ 80 % from scores of 35%–50% pre-operation (based on the Oxford Hip Score) ³.

Patient education and preoperative intervention are essential to optimizing TJA candidates for surgery as 80% of patients have at least one MRF ³⁸. Early screening helps identify these risks, and a multidisciplinary approach involving orthopedic surgeons and care teams is key to improving outcomes ^{29,38}.

Based on the gathered information regarding the health status of the Icelandic TJA cohort, it is possible to improve the implementation of preoperative optimization to increase efficiency for patients and the health care.

Implementation of structured preoperative optimization of MRFs should be the main goal of health care providers, with primary health care services at the center. Cooperation should be possible with hospitals when further consultations are needed and with specialist consultations in the private sector. Many patients have their own cardiologists, pulmonologists, endocrinologists, and nephrologists. This path has already been cleared, and it would be to patients' benefit to continue it.

Hospitals and private clinics could also take care of perioperative optimization. In the article "The Anesthesiologist as Public Health Physician," Moonesinghe highlighted the evolution of the anesthesiologist's role from ensuring immobility and pain relief since the first use of anesthesia in 1846 to minimizing short- and long-term surgical risks. With a holistic approach to perioperative care, anesthesiologists are well-positioned to lead the development of care pathways, identify and manage at-risk patients, and guide shared decision-making ¹¹⁴.

However, it seems to be of more benefit to the patient if preoperative optimization before TJA takes place within primary health care given that the approach is multifactorial, and information kept at one hand enabling future care and follow-up accessible for various health issues.

The method that will be chosen depends on which resources are at hand, and it is therefore also important to establish the effectiveness of optimization pathways. Patient-specific risk factors significantly influence the risk of superficial SSI and PJI. Shared decision-making, considering comorbidities and lifestyle, is key. Additionally, large RCTs, registry-based surveillance, and evidence-based guideline development are strongly encouraged ¹¹⁷.

In this case, hospitals, orthopedic surgeons, and anesthesiologists must communicate with primary health care. Patients' primary health care access must be secured, and specialist consultations should be accessible.

Genetic research into biofilms and the causes of diseases might also be in the future, giving information that might improve outcomes. Cao et al. stated that a multidisciplinary approach is essential in managing PJI. Future research should focus on developing antibiotics specifically targeting biofilm-producing bacteria and delivery systems that enhance biofilm penetration. Promising strategies include intra-articular antibiotic infusion, biofilm disruption or inhibition, and exploring the genetic and environmental factors involved in biofilm formation. Materials resistant

to biofilm adherence and technologies like ultrasound or radiofrequency for biofilm disruption also warrant development ¹¹⁷.

While 90% of OECD countries have an electronic health portal in place, only 42% have reported that the public could both access and interact with all their data through the portal ³.

Further research is needed to understand the role of genetics, comorbidities, and lifestyle in infection risk. Integrating AI and machine learning into clinical practice may improve diagnosis and treatment outcomes ¹¹⁷.

6 Conclusion

This project successfully enhanced patient engagement and improved MRFs through a structured preoperative optimization pathway involving coordinated efforts between hospitals and primary health care services. This optimization was associated with a reduction in overall surgical site complications and lower odds of superficial SSI in the intervention group. While optimizing patients before surgery is a rational approach, its impact must be rigorously evaluated. In this study, preoperative optimization did not lead to a significant reduction in superficial SSI at one year or PJI at three years. Incidence of long-term health-related diagnosis and acute health events up to three years after surgery was lower in the intervention group, though this finding was not significant. Post-operation admissions to hospital and mortality were similar between the groups. External factors, such as the relocation of TJA procedures and the disruptions caused by the COVID-19 pandemic, may have influenced patient selection and care, potentially affecting results. These findings highlight the need for long-term prospective studies on preoperative optimization and careful evaluation of how organizational and circumstantial changes impact patient outcomes.

Original publications

Paper I

Prevalence of modifiable risk factors in primary elective arthroplasty and their association with infections

M. Sigurdardottir, M. I. Sigurdsson, Y. Olafsson, S. H. Sverrisdottir, I. Gunnarsdottir, E. L. Sigurdsson, et al. Acta Orthop 2023 Vol. 94 Pages 38-44
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<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9893833/pdf/ActaO-94-8480.pdf>

Paper II

Preoperative optimization of modifiable risk factors is associated with decreased superficial surgical site infections after total joint arthroplasty: a prospective case-control study.

M. Sigurdardottir, M. I. Sigurdsson, R. D. Vias, Y. Olafsson, I. Gunnarsdottir, E. L. Sigurdsson, et al.
Acta Orthop 2024 Vol. 95 Pages 392-400
Accession Number: 39016247 PMCID: PMC11253708
DOI: 10.2340/17453674.2024.41012
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11253708/pdf/ActaO-95-41012.pdf>

Paper III

Prospective long-term follow-up of surgical complications and general health after preoperative optimization for primary arthroplasty

M. Sigurdardottir, M. I. Sigurdsson, R. D. Vias, Y. Olafsson, I. Gunnarsdottir, E. L. Sigurdsson, S. Karason submitted for publication 2025.

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Paper I

Prevalence of modifiable risk factors in primary elective arthroplasty and their association with infections

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Background and purpose — The aim of this study was to identify the prevalence of modifiable risk factors of surgical site infections (SSI) in patients undergoing primary elective total joint arthroplasty (TJA) receiving conventional pre-operative preparation, and to explore their association with infectious outcomes.

Patients and methods — Information regarding modifiable risk factors (anemia, diabetes, obesity, nutritional status, smoking, physical activity) was prospectively gathered in patients undergoing primary TJA of hip or knee in 2018–2020 at a single institution with 6 weeks' follow-up time.

Results — 738 patients (median age 68 years [IQR 61–73], women 57%) underwent TJA (knee 64%, hip 36%). Anemia was detected in 8%, diabetes was present in 9%, an additional 2% had undiagnosed diabetes (HbA1c > 47 mmol/mol), and 8% dysglycemia (HbA1c 42–47 mmol/mol). Obesity (BMI ≥ 30) was observed in 52%. Serum albumin, total lymphocyte count, and vitamin D below normal limits was identified in 0.1%, 18%, and 16%, respectively. Current smokers were 7%. Surgical site complications occurred in 116 (16%), superficial SSI in 57 (8%), progressing to periprosthetic joint infection in 7 cases. Univariate analysis identified higher odds of superficial SSI for BMI ≥ 30 (OR 2.1, 95%CI 1.2–3.8) and HbA1c ≥ 42 mmol/mol (OR 2.2, CI 1.1–4.2), but no association was found with other factors.

Conclusion — In a general population undergoing primary TJA an association was found between obesity (52%) and dysglycemia/diabetes (19%) and superficial SSI (8%), which progressed to PJI in 12% of cases, generating a 1% total rate of PJI. Modification of these risk factors might mitigate infectious adverse outcomes.

Superficial surgical-site infection (SSI) is a feared complication of total joint arthroplasty (TJA), occurring in 1–10% of cases. It may progress into periprosthetic joint infection (PJI), a devastating complication that occurs in between 0.5% and 2.4% of primary hip and knee TJAs (1,2). Several underlying medical conditions have been identified as independent risk factors for development of PJI that might be modified before operation (3). *Preoperative anemia* is present in up to 20% of patients undergoing elective TJA (4) and is associated with a higher rate of PJI, or 4.3% compared with 2% in non-anemic patients (3). *Diabetes mellitus* (Type I and II) has a prevalence of 8.5% worldwide (5) but may be present in up to 20% in patients undergoing TJA (6). The incidence of PJI for patients with diabetes is 1.6% and 2.2% after hip and knee arthroplasty compared with 0.7% and 0.5% in non-diabetic patients (3,7). *Obesity*, defined as body mass index (BMI) ≥ 30, carries increased risk for associated diseases, including diabetes (3) and osteoarthritis (8). The risk of PJI increases exponentially with increasing BMI (3) and PJI rates are reported to rise from 4.7% in patients with BMI > 40 to 9.8% if the patients are also diabetic, contrasted with 0.4% in patients with normal BMI (3,7). Laboratory screening of *nutritional status* in orthopedic surgery patients frequently includes serum albumin levels and total lymphocyte count (9) with risk of poor nutritional status associated with serum albumin level < 35 g/L, or total lymphocyte count < 1.5 × 10⁹/L. Both are independent risk factors for PJI (3). Additionally, vitamin-D deficiency is more common among patients whose surgery is complicated by PJI (10). *Smoking* is a significant risk factor for postoperative wound complications with a rate of SSI of 1.8% for current smoking at the time of TJA compared with 1.3% and 1.1% in former smokers or nonsmokers, respectively. Cessation of smoking

4–6 weeks prior to and after surgery decreases wound complications (3). Preoperative functional capacity and exercise are also considered an important predictor of postoperative outcome although their association with infectious outcome is unclear (11).

The primary aim of this study was to evaluate the prevalence of modifiable risk factors in patients undergoing primary TJA. The secondary aim was to assess their association with superficial SSI, with the purpose of creating a benchmark for interventional studies focusing on improving those factors.

Patients and methods

Study design, setting, and patient selection

This is a report of the control arm of a non-randomized open-label prospective quality control study evaluating outcome before and after an interventional effort to improve patient condition before TJA (Figure, see Appendix). All adult patients undergoing elective TJA who had received conventional preoperative preparation between August 2018 and September 2020 at Landspítali—the National University Hospital of Iceland in Reykjavik—were offered participation in the control arm of the study when visiting the hospital outpatient preoperative assessment clinic 1 week prior to surgery. 744 accepted and information on modifiable risk factors was gathered, additional blood tests were taken, and patients asked to answer a questionnaire regarding weight, anemia treatment, nutrition, smoking, physical activity, and involvement of healthcare providers in the months preceding the operation.

Procedure

Routine TJA at our institute are performed with spinal anesthesia; if not applicable, general anesthesia is administered. Prophylactic antibiotic treatment is provided with dicloxacillin, with the first dose given within 1 hour before surgery and repeated doses given 2 and 6 hours after surgery starts. Low molecular weight heparin is given as thromboprophylaxis, starting the evening before operation, and tranexamic acid is given during operation to decrease blood loss. Infiltration of ropivacaine at the surgical site is used for postoperative pain treatment in knee prosthesis patients. Drains are usually not inserted.

Clinical variables

Information was gathered regarding age, sex, smoking, comorbidities, type of surgery, type of anesthesia, ASA classification, laboratory values, blood transfusions, and length of stay.

Hemoglobin values were acquired 1 week prior to surgery and on the morning of the first postoperative day. Preoperative anemia was defined according to WHO's definition as a hemoglobin concentration of < 120 g/L and < 130 g/L in women and men, respectively (12), and divided into mild (110–120/130 g/L per sex), moderate (80–109 g/L), and severe (< 80 g/L).

A serum-glucose value was acquired 1 week prior to surgery and controlled on the morning of the 1st postoperative day. Patients were considered to have diabetes if they had received this diagnosis preoperatively or had a HbA1c level > 47 mmol/mol. Non-diabetic patients were considered to have dysglycemia if HbA1c was 42–47 mmol/mol and undiagnosed diabetes if HbA1c > 47 mmol/mol.

Patients were asked through questionnaire at the preoperative visit to estimate what their weight had been when surgery was decided on, and subsequently they were weighed. BMI was classified according to WHO's definition: < 18.5 underweight, 18.5–24.9 normal weight, 25–29.9 overweight, 30–34.9 obesity class I, 35–39.9 class II, and ≥ 40 class III (13).

Patients who had serum albumin < 35 g/L or lymphocyte count < 1.5×10^9 /L (9) were considered to be at risk of malnutrition. Vitamin-D deficiency was defined as 25OHD concentration < 50 nmol/L (14).

Information regarding smoking was gained from a questionnaire and divided into those who had quit smoking > 1 year ago, > 6 months ago, > 6 weeks ago, and < 6 weeks ago.

Patients were asked via questionnaire about their level of physical activity when waiting for operation and use of prescribed physical activity from primary healthcare and physiotherapy (15). Physical activity was divided into 2 classes, 0–2 times per week and 3–5 times per week. Each occasion was graded from 1 to > 60 minutes.

First planned instance of patient follow-up occurred 2–3 weeks postoperatively at primary care for suture removal and evaluation of surgical site complications. A 2nd routine follow-up occurred at the hospital orthopedic outpatient clinic 6 weeks postoperatively. Patient records from both primary care and hospital were reviewed to identify whether diagnosis of SSI (superficial or deeper) had been set or other complications had appeared. Diagnosis of superficial SSI was set according to the Centers for Disease Control and Prevention (CDC) definition of superficial SSI when clinical features were mentioned in medical notes of peri-incisional pain or tenderness, localized swelling, erythema, or heat and if antibiotics had been prescribed (16). Other signs of surgical site complications were also recorded such as drainage, bleeding, dehiscence, and hematoma. Referral to the hospital was in some cases direct after such diagnosis or later if the patient was not responding to treatment. In cases of deeper SSI or PJI involving the fascia, muscle layers and prosthesis, diagnosis was made by orthopedic surgeons according to evidence-based and validated criteria of periprosthetic hip and knee infection and confirmed with 5 tissue cultures during surgery with debridement, antibiotics, and implant retention (DAIR operation) (17).

Statistics

Patient demographics were described as median (interquartile range [IQR]) for continuous variables, and number (percentage) for categorical variables. Mean and standard deviation (SD) were reported for normally distributed data. The number

Table 1. Patient characteristics. Values are count (%) unless otherwise specified

Patient characteristics	Overall (N = 738)	Missing	Patient characteristics	Overall (N = 738)	Missing
Age in years, median [IQR]	68 [61–73]		Type of anesthesia		
Female sex	421 (57)		Spinal	659 (89)	
BMI when operation decided		136 (18)	General	79 (11)	
Median BMI [IQR]	31 [27–35]		ASA classification		
< 18.5	1 (0.1)		Class 1	44 (6)	
18.5–24.9	76 (10)		Class 2	528 (72)	
25–29.9	198 (27)		Class 3	164 (22)	
30–34.9	188 (26)		Class 4	2 (0.3)	
35–39.9	99 (13)		Blood tests		
40–44.9	30 (4)		Hemoglobin, g/L, mean (SD)		
45–49.9	8 (1)		preoperative	141 (13)	2 (0.3)
≥ 50	2 (0.3)		postoperative	116 (13)	34 (5)
BMI at operation		1 (0.1)	Hemoglobin dropp, mean (SD)	25 (11)	34 (5)
Median BMI [IQR]	30 [27–34]		Anemia preoperative ^a	56 (8)	2 (0.3)
<18.5	1 (0.1)		mild	47 (6)	
18.5–24.9	94 (13)		moderate	8 (1)	
25–29.5	258 (35)		severe	1 (0.1)	
30–34.9	238 (32)		Creatinine, μmol/L, mean (SD)		
35–39.5	108 (15)		preoperative	78.5 (23)	2 (0.3)
40–44.9	33 (4)		postoperative	81.4 (29)	34 (5)
45–49.9	5 (0.7)		Glucose, mmol/L, mean (SD)		
≥ 50	0 (0)		preoperative	6 (2)	13 (2)
Patient comorbidities		11 (1)	postoperative	7 (1)	38 (5)
Smoking	54 (7)		HbA1c, mmol/mol, mean (SD)		
Hypertension	401 (54)		preoperative	38.1 (8)	17 (2)
Ischemic heart disease	80 (11)		HbA1c, n (%)		
Arrhythmias	105 (14)		42–47 mmol/mol preoperative	52 (8)	
Anticoagulation preop	78 (11)		> 47 mmol/mol preoperative	13 (2)	
Congestive heart failure	13 (2)		Albumin, g/L, mean (SD)	44 (3)	12 (2)
Lung disease	131 (18)		Lymphocytes < 1.5x10 ⁹ /L, n (%)	129 (18)	2 (0.3)
Pulmonary embolism	7 (0.9)		Vitamin D nmol/L, mean (SD)	80 (34)	16 (2)
Deep vein thrombosis preop	10 (1)		Vitamin D < 50 nmol/L, n (%)	121 (16)	16 (2)
Diabetes	65 (9)		Blood transfusions	19 (3)	
Chronic renal failure	45 (6)		Days of stay, median [IQR]	1 [1–2]	
Transient ischemic attack	48 (7)		Postoperative complications		
Neuro bleeding	5 (0.7)		≤ 6 weeks from operation		
Inflammatory arthritis	50 (7)		Myocardial infarction	2 (0.3)	
Depression	73 (10)		Heart failure	3 (0.4)	
Anxiety	43 (6)		Pneumonia	7 (0.9)	
Cancer	78 (11)		Transient ischemic attack	1 (0.1)	
Type of operation			Pulmonary embolism	3 (0.4)	
Knee replacement	476 (65)		Deep vein thrombosis	3 (0.4)	
Hip replacement	262 (35)		Kidney failure	11 (1)	

^a Anemia severity: mild (110–120/130 g/L per sex), moderate (80–109 g/L) and severe (< 80 g/L)

of patients with a missing variable was reported, but variables were assumed to be missing at random.

A univariate association between the presence of the 5 modifiable risk factors and the presence of postoperative SSI was performed with logistic regression, estimating the odds and 95% confidence intervals (CI) of superficial SSI as a function of preoperative anemia, HbA1c ≥ 42 mmol/mol, BMI ≥ 30, smoking, vitamin D < 50 nmol/L, and physical activity.

As this was a descriptive study no assessment of power was performed prior to analysis.

All statistics were performed in R, version 1.3.1093 (Rstudio IDE) using Rstudio (R Foundation for Statistical Computing, Vienna, Austria).

Ethics, registration, funding, data sharing, and disclosures

The study was approved by the Science Committee of the Capital area's Primary Care and University of Iceland and by the Icelandic National Bioethics Committee (case number: VSN-18-098) and is registered at ClinicalTrials.gov (NCT05399186). This study was supported by grants from Landspítali Research Fund (A-2019-056, A-202-042, A-2021-036) and Research fund of Sigridur Larusdottir by University of Iceland. Data sharing is possible after reasonable request. The authors declare no conflict of interest. Completed disclosure forms for this article following the ICMJE template are available on the article page, doi: 10.2340/17453674.2023.8480

Table 3. Surgical site complications at 6 weeks follow up after operation. Values are count (%)

Surgical site complications	Overall (N = 738)	Missing
All	116 (16)	3 (0.4)
Superficial SSI	57 (8)	3 (0.4)
Drainage	58 (8)	3 (0.4)
Bleeding	42 (6)	3 (0.4)
Dehiscence	12 (2)	3 (0.4)
Limb hematoma	13 (2)	3 (0.4)
Periprosthetic joint infection	7 (1)	3 (0.4)
DAIR operation ^a	7 (1)	3 (0.4)

^a DAIR = Debridement, antibiotics and implant retention

Results

744 patients accepted to participate but 6 were excluded (2 with contraindication to surgery and 4 had surgery in another joint). Thus, 738 patients, 69% of all eligible TJA patients, were included in the study (Figure, see Appendix). For patient characteristics, comorbidities, ASA classification, and anesthesia technique see Table 1, for results from questionnaires see Table 2 (see Appendix), and for postoperative surgical site complications see Table 3. Within 6 weeks postoperatively 26 (4%) patients had suffered other complications, but no deaths had occurred (Table 1).

The mean value of preoperative hemoglobin was 141 g/L (SD 13) but anemia was detected in 56 (8%) patients (Table 1) and 22 (3%) reported taking iron supplementation (Table 2, see Appendix). Perioperative blood transfusion was given to 19 (3%) patients with a median of 2 units (range 1–6) (Table 1), of whom 47% were anemic preoperatively.

The mean value of HbA1c was 38 mmol/mol (SD 8). A previous diagnosis of diabetes had been made in 65 (9%) of the patients. Among the non-diabetic patients, 52 (8%) had dysglycemia with HbA1c 42–47 mmol/mol and 13 (2%) patients had undiagnosed diabetes with HbA1c > 47 mmol/mol (Table 1).

At the time of decision for operation 44% of patients reported their BMI ≥ 30 according to the questionnaire. At the time of operation 52% had BMI ≥ 30 (Table 1).

The mean concentration of albumin was 44 g/L (SD 3) with 1 individual (0.1%) just below 35 g/L. The mean value of lymphocytes was 2×10⁹/L with 129 (18%) having a count below 1.5×10⁹/L. The mean value of Vitamin D was 80 nmol/L (SD 34) while 16% were below 50 nmol/L and considered deficient (Table 1).

Current smoking at the time of operation was reported by 54 (7%) of the patients (Table 2, see Appendix).

According to the questionnaire, 68% of patients had tried to increase their physical activity while waiting for surgery while motion occasions per week were estimated to be none by 15% of patients. Preoperative use of prescribed physical activity from primary healthcare occurred in 6% and 27% had received treatment by a physiotherapist (Table 2, see Appendix).

Table 4. Odds ratio (OR) and (95% confidence interval) of superficial SSI for patients with preoperative risk factors

Superficial SSI	OR (95% CI)	Missing
Preoperative anemia	0.91 (0.27–2.3)	2
HbA1c ≥ 42 mmol/mol	2.2 (1.1–4.2)	17
BMI at operation ≥ 30	2.1 (1.2–3.8)	1
Smoking	1.2 (0.41–3.0)	11
Vitamin D ≤ 50 nmol/L	0.85 (0.38–1.7)	16
Weekly motion ≤ 2	1.4 (0.73–2.6)	71

58 of the patients (8%) had visited a primary care physician preoperatively and 90 (12%) had received a consultation from a cardiologist (Table 2, see Appendix).

Surgical site complications occurred in 116 (16%) of the patients (Table 3), including superficial SSI in 57 (8%) and 7 of these progressed to PJI, generating a rate of 1% PJI. Reoperation due to PJI with debridement, antibiotics, and implant retention (DAIR operation) was performed in all 7. Cultures were taken in 49% of SSI cases, including all PJI, of which 64% were positive. Staphylococci were the pathogen in 95% of cases and Pseudomonas in 5%.

An exploratory secondary analysis was performed to assess the correlation between preoperative modifiable risk factors and postoperative superficial SSI. This revealed higher odds of superficial SSI for BMI ≥ 30 (OR 2.1, CI 1.2–3.8) as well as HbA1c ≥ 42 mmol/mol (OR 2.2, CI 1.1–4.2). No association was found with other factors (Table 4).

Discussion

In this study of patients undergoing primary TJA after conventional preoperative preparation the rates of several known modifiable risk factors for adverse infectious outcomes were in the lower range of previous studies but superficial SSI in the higher. An association was found between elevated BMI and HbA1c and superficial SSI.

In recent years the advantage of optimizing the patient's condition before an elective TJA has been emphasized for the benefit of the patient and healthcare systems (3,18). Selection of patients for such intervention and what methods to use are not clear though. Improvements in modifiable risk factors might be unobtainable in individual patients or the efforts required to attain a general modification of them and the amount of decrease in negative outcome so small that they are uneconomical. This study might lay the ground for evaluation of such interventional studies on preoperative optimization.

The patient group was comparable with other studies in regard to age, sex ratio, ASA classification, length of hospital stay, and ratio between total hip (36%) and total knee arthroplasty (64%) (8,19). Neuraxial anesthesia was used in

the majority of cases (89%), as generally recommended, but may vary between institutions (20).

The prevalence of preoperative anemia was 8%, considerably lower than the 15–30% reported in previous studies (4). However, only 3% had received treatment for anemia, suggesting that a preoperative blood management program could have been beneficial. The drop in hemoglobin at postoperative day 1 was 26 g/L and only 3% (19 patients) received blood transfusion, comparable with a recent study with the same drop in hemoglobin and a transfusion rate of 4% (21).

In our cohort 9% of the patients had been diagnosed with diabetes, which is slightly higher than the 8.3% in the general population of Iceland (22). Of the non-diabetic patients, 8% had dysglycemia and 2% had undiagnosed diabetes. The prevalence of diagnosed diabetes varies substantially between countries and therefore also in studies on TJA, or between 6% and 12%, as does undiagnosed diabetes, or up to 41% (23,24).

At the time of decision for operation, 44% of the patients self-reported their BMI as ≥ 30 but at operation 52% were measured with BMI ≥ 30 . It is questionable how reliably individuals estimate their own weight, but the information possibly points to weight gain during wait for operation. The distribution of BMI classes at operation was comparable with a recent study from the USA (25). Guidelines support weight reduction to decrease risk of PJI, but there is no consensus on what method to use to induce weight loss (18,26).

The prevalence of poor nutritional status estimated by low levels of albumin and lymphocytes was very infrequent compared with previous studies (9,10), pointing towards a good nutritional status of the patients in general, except that 16% were defined as being vitamin-D deficient, ranging from 13–80% in the USA with prevalence of 42% (10).

The prevalence of smoking was reported by the patients to be 7%, which is the same as in society in general (27); 39% had stopped smoking > 1 year ago and 3% within a year but missing data were noted from 59%.

Two-thirds of the patients reported that they had tried to increase their physical activity during the wait for operation and half exercised 3–5 times per week, but 15% reported no motion at all. Utilization of prescribed physical activity from primary health care (15) followed by digital communication and physiotherapy was relatively low. It therefore seems that the general physical status of patients could be improved with more purposeful pre-habilitation (Tables 4 and 2, see Appendix) (11).

Surgical site complications were identified in 16% of the patients, which is higher than in previous reports of 5.5–14.3% (28), although definitions likely vary.

Superficial SSI occurred in 8%, which is higher than the 1% to 2.5% reported from the USA (29) but similar to the 7% in Sweden (1). We identified an association with elevated BMI and HbA1c. With the high number of patients with BMI ≥ 30 and patients with elevated HbA1c without a diagnosis of diabetes (Tables 1 and 4), perhaps targeting these risk factors would be most likely to result in a reduced rate of SSI.

Superficial SSI progressed to PJI in 7 of 57 (12%) cases, which is lower than in a recent report from Sweden where the progression rate was 29%. However, their follow-up time was slightly longer than was used in our study (1).

PJI occurred in 7 patients (1%), 5 total knee and 2 total hip arthroplasties, which is within the range as compared with other studies or 0.5–2.5% and with the 1.45% PJI rate recently reported from the Swedish Knee Arthroplasty Register (2,30). All progressed from superficial SSI, and reoperation with debridement, antibiotics, and implant retention (DAIR operation) was necessary in all cases.

Examination of the surgical wound and removal of sutures occurred 2 weeks after the operation at primary care. This was, though, changed at the end of the study as orthopedic surgeons became aware of the high incidence of superficial SSI after a preliminary report from the study, and the last 17 patients in the knee arthroplasty group were followed up at the hospital outpatient clinic. None of those were diagnosed with a superficial SSI, which might indicate a difference in interpretation of infectious signs or improved performance of orthopedic surgeons. A visit to the hospital orthopedic outpatient clinic for clinical evaluation 6 weeks after operation occurred in 99% of cases. For the remaining 1% information at 6 weeks postoperatively was gathered from medical notes, either from primary care or hospitals and rehabilitations centers where patients had been admitted, so no patient was lost to follow-up.

Limitations

The foremost limitation of the study is a rather low number of patients, causing a challenge to identify modifiable risk factors of SSI. Also, the follow-up time of 6 weeks is rather short allowing only study of acute development of PJI.

Strengths

The main strength of this study is detailed prospective gathering of data, thorough follow-up and very low ratio of missing clinical data. No selection was performed due to health status or comorbidities and a high ratio of eligible patients (69%) were included. The demographics of the patient group are similar to other studies, allowing the results to be compared with them.

Conclusion

In this study of a general population undergoing primary TJA after conventional preoperative preparation the prevalence of several known modifiable risk factors was generally in the lower range and deviations in these not as severe as in previous reports. However, obesity was present in 52% and dysglycemia and diabetes together in 19%. An association was found between obesity (BMI ≥ 30) and elevated HbA1C (> 42 mmol/mol) and superficial SSI (8%), which progressed to PJI in 12% of cases, generating a 1% total rate of PJI in the patient group after 6 weeks' follow-up. This may indicate that focus on these modifiable risk factors might mitigate infectious adverse outcomes after primary TJA.

This study will lay the ground for an interventional study of preoperative improvement before TJA.

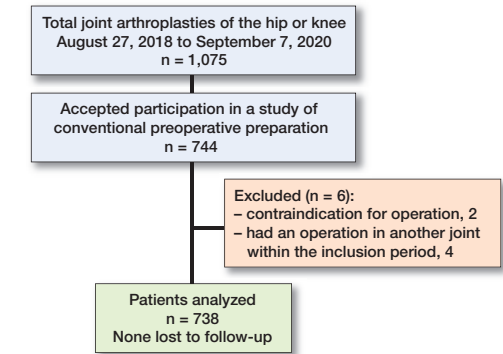
MS: study initiation and design, data collection, data analysis, manuscript writing. MIS: data analysis, interpretation of data, manuscript writing. YO: study design, manuscript writing. SHS: inclusion of patients, manuscript writing. IG: study design, interpretation of data, manuscript writing. ELS: interpretation of data, manuscript writing. SK: Study initiation and design, data analysis and interpretation, manuscript writing.

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Appendix



Consort flow diagram.

Table 2. Answers to questionnaire at preoperative visit. Values are count (%)

Answers	Yes	Not applicable	Missing
During wait for surgery have you been informed of following health factors and possible influence of them on the outcome of the operation?			
Weight	321 (44)	130 (18)	21 (3)
Motion	381 (52)	112 (15)	18 (2)
Nutrition	281 (38)	138 (19)	27 (4)
Smoking	182 (25)	320 (43)	27 (4)
Still smoking at time of surgery	54 (7)		11 (2)
Anemia	83 (11)	257 (35)	59 (8)
During wait for surgery have you tried to influence the following health factors?			
Weight	440 (60)	54 (7)	31 (4)
Motion	500 (68)	45 (6)	27 (4)
Use of			
primary care prescribed			
physical activity	42 (6)		486 (66)
physiotherapy	201 (27)		388 (53)
Motion incidences/week			71 (10)
0	114 (15)		
1	49 (7)		
2	131 (18)		
3	158 (21)		
4	93 (13)		
≥ 5	122 (17)		
Motion length, minutes			78 (11)
0	101 (14)		
0–20	117 (16)		
20–40	200 (27)		
40–60	170 (23)		
> 60	72 (10)		
Nutrition	440 (60)	57 (8)	34 (5)
Smoking	102 (14)	450 (61)	66 (9)
Still smoking at time of surgery	54 (7)	11 (2)	
If previous smoker when did you quit?			434 (59)
< 6 weeks	6 (0.8)		
6 weeks to < 6 months	6 (0.8)		
6 months to < 1 year	6 (0.8)		
≥ 1 year	286 (39)		
Anemia			
(treatment with iron)	22 (3)	323 (44)	90 (12)
During wait for surgery have you been in contact with other health care providers?			
Cardiologist	90 (12)	147 (20)	77 (10)
Pulmonologist	25 (3)	180 (24)	90 (12)
Diabetologist	14 (2)	206 (28)	90 (12)
Nephrologist	9 (1)	207 (28)	93 (13)
Primary care	58 (8)		102 (14)

Paper II

Preoperative optimization of modifiable risk factors is associated with decreased superficial surgical site infections after total joint arthroplasty: a prospective case-control study

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Background and purpose — The aim of our study was to investigate change in modifiable risk factors following preoperative optimization and whether risk of superficial surgical site infection (SSI) after total joint arthroplasty (TJA) could be reduced.

Methods — This is a prospective study of implementation of a preoperative optimization pathway for patients waiting for primary TJA. Information regarding the intervention arm was collected from January 2019 to January 2021, first at decision for operation and then at preoperative assessment 1 week prior to operation. The control arm was included between August 2018 and September 2020 after receiving conventional preoperative preparation and information gathered at preoperative assessment. Follow up occurred 6 weeks postoperatively for both groups. The primary outcome was postoperative superficial SSI.

Results — The optimization effort resulted in improvement of weight, anemia, HbA1c, vitamin D, and patient engagement. At preoperative assessment the baseline characteristics of the 2 groups were similar except that the intervention group had substantially more comorbidities. Regarding superficial SSI, association was found with BMI ≥ 30 and HbA1c ≥ 42 mmol/mol in the control group but not in the intervention group. When corrected for differences in ASA classification (reflecting comorbidities), age, and sex, being in the intervention group was associated with lower odds of occurrence of superficial SSI compared with the control group (OR 0.64, 95% confidence interval 0.42–0.97).

Conclusion — We showed that preoperative optimization in a structured cooperation between hospital and primary care was associated with a reduced risk of superficial SSI.

There are several well-known modifiable risk factors that increase risk of periprosthetic joint infections (PJI) after total joint arthroplasty (TJA). These include anemia, dysglycemia/diabetes, obesity, poor nutritional status, smoking [1] and possibly reduced physical capacity [2].

There is increasing interest in preoperative optimization to decrease risk of postoperative complications, especially infections as they reduce quality of life substantially for patients and increase costs extensively [3,4].

The structure of such preoperative optimization programs has varied and they are either hospital or primary care centered or include cooperation between the 2 organizations [5–7]. The choice of which risk factors are optimized varies considerably, as well as what target is set to be obtained [8]. Little has been published regarding the design, implementation, or efficacy of such programs [9,10].

The aim of our study was to evaluate change in modifiable risk factors after preoperative optimization. Moreover, we investigated its association with the incidence of postoperative superficial surgical site infection (SSI) compared with conventional preparation.

Methods

This is a prospective case control study evaluating outcome of an intervention effort to improve patients' modifiable risk factors as compared with conventional preoperative preparation before primary TJA at a single institution. The study was conducted according to the STROBE guidelines for observational studies.

The routines of TJA surgery, nature of information gathered, variables collected, definitions used, and how patients were categorized have previously been described [11]. In short, data collection included age, gender, weight, comorbidities, surgery and anesthesia type, ASA classification, various laboratory variables, blood transfusions, and length of stay. BMI was classified according to the WHO's definition, encompassing different weight categories. Diabetes status was determined by preoperative diagnosis or HbA1c levels. Non-diabetic patients were considered to have dysglycemia if HbA1c was 42–47 mmol/mol and undiagnosed diabetes if HbA1c > 47 mmol/mol. Preoperative anemia was defined based on WHO's criteria for hemoglobin concentration (< 120 g/L in women and < 130 g/L in men). Patients at risk of malnutrition were identified by low serum albumin or lymphocyte count. Vitamin-D deficiency was defined by 25-OH-D concentration < 50 nmol/L. Due to costs, only patients with vitamin-D value < 50 nmol on decision for operation had a repeated measurement 1 week prior to operation. Engagement, physical activity, smoking history, and program satisfaction was assessed with questionnaires.

Intervention group, optimization of patient pathway

We started in 2017 to improve modifiable risk factors utilizing the waiting time of patients before TJA at Landspítali, the National University Hospital of Iceland. Support of hospital and primary health care directors was gained, and agreement made with primary care physicians. Information meetings were held at the various primary health care centers involved. An optimization patient pathway was designed and routes of communication between parties decided, including primary care physicians, hospital orthopedic outpatient clinic, preoperative assessment center, department of clinical nutrition, and specialist outpatient services.

After a pilot trial, inclusion in the intervention started in January 2019 and continued until January 2021, and the patients were operated on from March 2019 to December 2022. The COVID-19 pandemic caused some disruption of planning.

The patients were offered participation 6–12 months prior to surgery at the hospital orthopedic outpatient clinic after being referred there by their primary care physician. If willing to participate, baseline blood tests were taken, and BMI registered. An appointment with their primary care physician was booked within 3 weeks to evaluate results of blood test and assess whether further tests, treatments, or consultations were necessary, focusing on obesity, glycemic control, anemia, nutritional status, smoking cessation, and exercise.

Patients with BMI ≥ 40 received a phone call from a hospital-based clinical nutritionist and were offered a personal interview where general advice regarding food intake was given. Patients with vitamin D < 50 nmol/L received 1 phone call from a hospital-based nutritionist with recommendations for daily doses of vitamin-D supplements based on serum concentration value and weight with the aim to reach a concentration

of 75 nmol/L prior to operation, preferably within 3 months [12]. Patients were instructed to continue to take the supplements until the operation. Risk of malnutrition was assessed using a validated screening tool [13] and those defined to be at risk received a consultation.

1 week prior to surgery the patients were re-evaluated at the hospital preoperative assessment clinic, and were asked to answer a questionnaire regarding anemia treatment, nutrition, smoking, physical activity, involvement of healthcare providers in the months preceding the operation, will to influence modifiable risk factors, and awareness of the preoperative optimization efforts and satisfaction with the process.

Control group

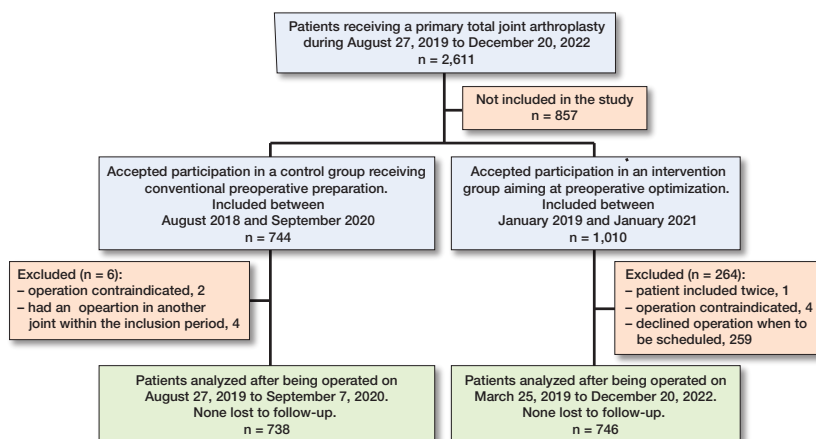
The patients in the control group were already on the waiting list for TJA when the study started and had received conventional preoperative preparation, which consisted of general recommendations from the orthopedic surgeon regarding weight, smoking, and lifestyle on decision for operation, with no further follow-up. Inclusion occurred between August 2018 and September 2020 at the hospital outpatient preoperative assessment clinic 1 week prior to surgery. If they accepted participation in the study the same evaluation occurred as in the intervention group and a questionnaire was answered.

Follow-up

Follow up was the same for both groups. Patients who had a total hip arthroplasty (THA) were assessed 2–3 weeks postoperatively in primary care for suture removal and evaluation of surgical site complications, while all total knee arthroplasty (TKA) patients were referred to the hospital orthopedic outpatient clinic as they were considered at higher risk of SSI. All patients were offered a 6-week postoperative follow-up visit at the hospital orthopedic outpatient clinic. Patient records from primary care and hospitals were reviewed to identify diagnoses of superficial or deeper surgical site infections and other complications. Superficial SSIs were diagnosed according to CDC criteria based on clinical features of peri-incisional pain, tenderness, swelling, erythema, heat, and antibiotic prescriptions [14]. Other recorded complications were drainage, bleeding, dehiscence, and hematoma. Deeper SSIs or periprosthetic joint infections (PJI) involving fascia, muscle layers, and prostheses were diagnosed by orthopedic surgeons using validated criteria and confirmed with 5 tissue cultures during a DAIR operation (debridement, antibiotics, and implant retention) [15].

Statistics

Group sizes were evaluated after analyzing prevalence of superficial SSI in the first 100 patients in the control group identifying 8 patients diagnosed with superficial SSI. These results were presented at the congress of the Icelandic Society of Anesthesia and Intensive Care Medicine, 2019. We estimated that optimization of modifiable risk factors could



Patient flow chart

reduce superficial SSIs from 8% to 4%, and this would require patient groups of 550 in each arm for comparisons, but our initial plan was to reach 1,000.

A Shapiro–Wilk test was used to assess normality of data. The Newcombe Score method was used to compute confidence intervals for the differences in proportions in 2-sample and paired-sample nominal data. When comparing differences in mean values of 2-sample and paired-sample continuous data, a Gaussian assumption was in no case reasonable, thus, bias-corrected and accelerated bootstrap confidence intervals were computed. When evaluating the differences between the groups the reference value for the significance of the 95% confidence interval (CI) is zero.

A univariate logistic regression analysis was used to measure association between patient characteristics and the occurrence of superficial SSI in the intervention group. A multivariable logistic regression analysis was used to measure association between the intervention and superficial SSI while adjusting for age, sex, and ASA classification. When evaluating the odds ratios the reference value for the significance of the 95% CI is 1.

The data analysis was done using R (version 4.2.2; R Foundation for Statistical Computing, Vienna, Austria). Missing data was below 3% in all clinical variables. In answers to questionnaires, missing data were between 2.4% and 65.9%. No imputation was performed.

Ethics, registration, funding, and disclosures

The study was approved by the Science Committee of the Capital Area's Primary Care and the University of Iceland and by the Icelandic National Bioethics Committee (case number: VSN-18-098) and registered at ClinicalTrials.gov (NCT05399186). Support was provided by grants from the Landspítali Research Fund (A-2019-056, A-202-042, A-2021-036) and the Research Fund of Sigríður Larusdóttir by the University of Iceland. Data sharing is possible upon reasonable request. The authors declare no

conflict of interest. Complete disclosure of interest forms according to ICMJE are available on the article page, doi: 10.2340/17453674.2024.41012

Results

Between August 2018 and December 2022, 2,611 patients received a primary TJA in our department. Between August 2018 and September 2020, 744 patients accepted to participate in the control group but 6 were excluded, thus 738 patients or 69% of eligible TJA patients were included. Between January

2019 and January 2021, 1,010 patients accepted to participate in the intervention arm but 264 were excluded, mostly ($n = 259$) because they declined operation when this was to be scheduled. Thus, 746 patients were included, or 43% of eligible TJA patients (Figure).

Optimization in the intervention group

The mean length of wait for operation for the intervention group was 356 days (standard deviation [SD] 223). Mean BMI decreased slightly (difference -0.4 , CI -0.6 to -0.3) but most notably in those with BMI ≥ 40 on decision for operation (difference -2.4 , CI -3.9 to -1.0). Among patients with BMI ≥ 40 , 90% received consultation regarding weight loss (40 from a hospital-based clinical nutritionist, 11 from primary care, 6 underwent bariatric surgery, 4 were treated at centers with weight loss programs). Other indices that improved were anemia (difference -1.5 , CI -3.4 to 0.4), HbA1c (difference -0.4 , CI -0.7 to -0.1), and vitamin D (difference 34.7 , CI 28.6 to 41.5), where 92% of those with deficiency received consultation and increased their mean value from 36 to 71 nmol/L 1 week before operation (difference 34.7 CI 28.6 to 41.5) (Table 1).

Comparison of intervention and control group

The 2 groups were similar regarding age, sex ratios, BMI distribution, type of operation and anesthesia, length of stay, and laboratory values. However, the intervention group had a higher ratio of several preoperative comorbidities in general, such as various heart diseases, anticoagulation treatment, renal insufficiency, and the ratio of diabetes was also higher in the intervention group, or 12.5% versus 8.8% (difference 3.7%, CI 0.5–6.8). This was reflected in a higher ratio of patients with ASA ≥ 3 classification or 32% versus 23% (difference 9.1%, CI 4.6–13.6). Postoperative medical complications within the first 6 weeks after operation were generally uncommon in both groups and no deaths occurred (Table 2).

Table 1. Intervention group, patient characteristics (N = 746) at 2 timepoints: on decision for operation and 1 week prior to it. Difference between the 2 timepoints is calculated between means when presented, otherwise between proportions (shown in parentheses) and is presented with 95% confidence interval. Values are count (%) unless otherwise specified

Patient characteristics of intervention group	On decision for operation	Missing	1 week prior to operation	Missing	Difference [CI]
Days waiting ^a			355 (223)	0 (0)	
Age ^a			67.9 (9.7)	0 (0)	
Female sex			414 (55)	0 (0)	
BMI ^a	31.4 (5.8)		31.0 (5.4)		−0.4 [−0.6 to −0.3]
< 18.5	1 (0.1)		1 (0.1)		0.0 [−0.5 to 0.5]
18.5–24.9	94 (13)		102 (14)		1.1 [−0.3 to 2.5]
25–29.9	228 (31)		231 (31)		0.4 [−1.8 to 2.6]
30–34.9	236 (32)		241 (32)		0.7 [−1.8 to 3.1]
35–39.9	124 (17)		126 (17)		0.3 [−2.0 to 2.5]
40–44.9	46 (6.2)		39 (5.2)		−0.9 [−2.5 to 0.6]
45–49.9	15 (2.0)		6 (0.8)		−1.2 [−2.4 to −0.3]
≥ 50	2 (0.3)		0 (0)		
Nutritionist consultation ^b					
BMI ≥ 40	63 (8.4)		45 (6.0)		−2.4 [−3.9 to −1.0]
Hemoglobin, g/L ^a	141.4 (12.8)	1 (0.1)	140.9 (12.6)		−0.6 [−1.2 to 0.1]
Anemia	55 (7.4)	1 (0.1)	44 (5.9)	0 (0)	−1.5 [−3.4 to 0.4]
Mild	46 (6.2)		38 (5.1)		−1.1 [−3.1 to 0.9]
Moderate	9 (1.2)		6 (0.8)		−0.4 [−1.5 to 0.6]
Severe	0 (0)		0 (0)		0.0 [−0.5 to 0.5]
Creatinine, μmol/L ^a	82.7 (41.6)	2 (0.3)	83.9 (47.7)		1.1 [0.1 to 2.2]
Glucose, mmol/L ^a	6.0 (1.3)	2 (0.3)	6.4 (1.5)	1 (0.1)	0.3 [0.2 to 0.4]
HbA1c, mmol/mol ^a	38.2 (7.6)	3 (0.4)	37.8 (7.3)	7 (0.9)	−0.4 [−0.7 to −0.1]
HbA1c for non-DM patients		2 (0.3)		7 (1.1)	
42–47 mmol/mol	46 (6.2)		49 (6.6)		0.5 [−1.7 to 2.7]
> 47 mmol/mol	6 (0.8)		8 (1.1)		0.3 [−0.7 to 1.4]
Albumin, g/L ^a	45.0 (2.7)	3 (0.4)	43.4 (2.7)	10 (1.3)	−1.6 [−1.8 to −1.4]
Albumin < 35 g/L	1 (0.1)	3 (0.4)	1 (0.1)	10 (1.3)	0.0 [−0.6 to 0.6]
Lymphocytes < 1.5x10 ⁹ /L	106 (14)	1 (0.1)	79 (11)	1 (0)	−3.6 [−6.3 to −1.0]
Vitamin D, nmol/L ^a	84.7 (34.5)	5 (0.7)			
Nutritionist consultation ^b					
Vitamin D < 50 on decision, nmol/L ^a	36.2 (9.3)		70.9 (28)		34.7 [28.6 to 41.5]

^a Values are mean (SD)

^b Individuals who had BMI ≥ 40 and those with vitamin D < 50 nmol/L on decision for operation received a nutritionist consultation on decision for operation. The change in number of patients with BMI ≥ 40 is shown at the 2 different timepoints and the change in mean vitamin D for the group that had < 50 nmol/L on decision for operation.

Results from the questionnaire 1 week prior to operation showed that the intervention group had a substantially higher level of awareness of modifiable risk factors than the control group and tried to a higher extent to influence them. A high ratio of patients followed the planned optimization pathway and visited their primary care physician after preoperative evaluation, i.e., 93%, but only 7.9% in the control group (difference 85%, CI 82 to 88). The intervention arm also more often visited other healthcare providers before the operation (Table 3, see Appendix). The intervention group was either satisfied or very satisfied with the hospital service, i.e., 65% (missing answers 13%), while this was 34% for primary care (missing answers 48%). Only 15% in the intervention group considered themselves either aware or well aware of the cooperation between hospital and primary care during the wait for operation, with 30% missing answers (Table 4, see Appendix).

Surgical site complications

In both groups over 95% attended a follow-up visit at the hospital orthopedic outpatient clinic 6 weeks after operation; others were followed by primary care, were admitted to hospital at the time, or received a phone call from the surgeon. No patient was lost to follow-up.

All complications gathered from the surgical site were lower in the intervention group at 11.3% versus 15.7% (difference −4.5%, CI −8.0 to −1.0) (Table 5). Superficial SSIs were less common in the intervention group at 5.6% versus 7.7% (difference −2.1%, CI −4.7 to 0.4). PJI developed in all cases from superficial SSI and occurred in 1.5% of cases in the intervention group but 0.9% in the control group (difference 0.5%, CI −0.7 to 1.8).

Regarding superficial SSI, staphylococci were the pathogen in 86% of cases in the intervention group and 95% in the control group (Table 6, see Appendix).

A univariable logistic regression analysis in the intervention group was unable to establish an association between superficial SSI and the presence of known preoperative risk factors (anemia, HbA1c > 42 mmol/mol, BMI ≥ 30, smoking, vitamin D < 50 nmol/L, weekly motion occasions < 2) 1 week prior to operation (Table 7).

In a multivariable logistic regression analysis adjusting for ASA classification (reflecting comorbidities), age, and

sex, being in the intervention group was associated with lower odds of superficial SSI compared with being in the control group (OR 0.64, CI 0.42–0.97) (Table 8).

Discussion

The aim of our study was to explore whether preoperative optimization of modifiable risk factors could mitigate infection outcomes after TJA. We found that with structured cooperation between hospital and primary health care it is possible to utilize the time while waiting for operation to improve patients' modifiable risk factors before TJA and reduce the odds of developing superficial SSI compared with a control group receiving a conventional preoperative preparation.

The choice to use superficial SSI as a primary outcome instead of PJI, which we did because of a low number of patients, may

Table 2. Comparisons of parameters of control and intervention groups 1 week prior to operation, perioperatively and 6 weeks postoperatively. Difference between the 2 groups is calculated between means when presented, otherwise between proportions (shown in parentheses) and is presented with 95% confidence interval. Values are count (%) unless otherwise specified

Patient characteristics 1 week prior to operation	Intervention group (n = 746)	Missing	Control group (n = 738)	Missing	Difference [CI]
Age ^a	67.9 (9.7)		66.7 (8.8)		1.2 [0.3 to 2.2]
Female sex	414 (55)		421 (57)		−1.6 [−6.6 to 3.5]
BMI ^a	31.0 (5.4)		30.6 (5.2)	1 (0.1)	0.4 [−0.2 to 0.9]
< 18.5	1 (0.1)		1 (0.1)		0.0 [−0.6 to 0.6]
18.5–24.9	102 (14)		94 (13)		0.9 [−2.5 to 4.4]
25–29.9	231 (31)		258 (35)		−4.0 [−8.8 to 0.7]
30–34.9	241 (32)		238 (32)		0.0 [−4.7 to 4.8]
35–39.9	126 (17)		108 (15)		2.2 [−1.5 to 5.9]
40–44.9	39 (5.2)		33 (4.5)		0.8 [−1.5 to 3.0]
45–49.9	6 (0.8)		5 (0.7)		0.1 [−0.9 to 1.1]
≥ 50	0 (0)		0 (0)		0.0 [−0.5 to 0.5]
Patient comorbidities					
Smoking	28 (3.8)	10 (1.3)	54 (7.3)	11 (1.5)	−3.6 [−6.1 to −1.3]
Hypertension	465 (62)		401 (54)		8.0 [3.0 to 13.0]
Ischemic heart disease	120 (16)		80 (11)		5.2 [1.8 to 8.7]
Arrhythmias	122 (16)		105 (14)		2.1 [−1.5 to 5.8]
Anticoagulation	113 (15)		78 (11)		4.6 [1.2 to 8.0]
Congestive heart failure	30 (4.0)		13 (1.8)		2.3 [0.5 to 4.1]
Lung disease	133 (18)		131 (18)		0.1 [−3.8 to 4.0]
Pulmonary embolism	26 (3.5)		7 (0.9)		2.5 [1.1 to 4.2]
Deep vein thrombosis	27 (3.6)		10 (1.4)		2.3 [0.7 to 4.0]
Diabetes	93 (13)		65 (8.8)		3.7 [0.5 to 6.8]
Renal insufficiency	82 (11)		45 (6.1)		4.9 [2.1 to 7.8]
Transient ischemic attack	42 (5.6)		48 (6.5)		−0.9 [−3.3 to 1.6]
CNS bleeding	4 (0.5)		5 (0.7)		−0.1 [−1.1 to 0.8]
Inflammatory arthritis	51 (6.8)		50 (6.8)		0.1 [−2.5 to 2.7]
Depression	78 (11)		73 (9.9)		0.6 [−2.5 to 3.7]
Anxiety	62 (8.3)		43 (5.8)		2.5 [−0.1 to 5.1]
Cancer	94 (13)		78 (11)		2.0 [−1.2 to 5.3]
Type of operation					
Knee replacement	480 (64)		476 (65)		−0.2 [−5.0 to 4.7]
Hip replacement	266 (36)		262 (36)		0.2 [−4.7 to 5.0]
Type of anesthesia					
Spinal	691 (93)		659 (89)		3.3 [0.4 to 6.3]
General	55 (7.4)		79 (11)		−3.3 [−6.3 to −0.4]
ASA classification					
Class 1	41 (5.5)		44 (6.0)		−0.5 [−2.9 to 1.9]
Class 2	469 (63)		528 (72)		−8.7 [−13.4 to −3.9]
Class 3	236 (32)		164 (22)		9.4 [4.9 to 13.9]
Class 4	0 (0)		2 (0.3)		−0.3 [−1.0 to 0.3]
ASA ≥ 3	236 (32)		166 (23)		9.1 [4.6 to 13.6]
Hemoglobin, g/L ^a					
Preoperative ^a	140.9 (12.6)		141.3 (13.4)	2 (0.3)	−0.4 [−1.8 to 0.9]
Postoperative ^a	112.9 (12.7)	4 (0.5)	115.9 (12.8)	34 (4.6)	−3.0 [−4.4 to −1.7]
Postoperative drop ^a	28.0 (8.4)	4 (0.5)	25.8 (10.9)	34 (4.6)	2.2 [1.2 to 3.2]
Anemia preoperative	44 (5.9)	0 (0)	56 (7.6)	2 (0.3)	−1.7 [−4.3 to 0.9]
Mild	38 (5.1)		47 (6.3)		−1.3 [−3.7 to 1.1]
Moderate	6 (0.8)		8 (1.1)		−0.3 [−1.4 to 0.8]
Severe			1 (0.1)		−0.1 [−0.8 to 0.4]
Creatinine, μmol/L ^a					
Preoperative	83.9 (47.7)		78.5 (22.6)	2 (0.3)	5.4 [2.5 to 10.7]
Postoperative	85.7 (56.0)	5 (0.7)	81.4 (29.3)	34 (4.6)	4.3 [0.6 to 10.3]
Glucose, mmol/L ^a					
Preoperative	6.4 (1.5)	1 (0.1)	6.1 (1.5)	13 (1.8)	0.3 [0.1 to 0.4]
Postoperative	6.5 (1.2)	12 (1.6)	6.8 (1.3)	38 (5.1)	−0.3 [−0.4 to −0.2]
HbA1c, mmol/L ^a					
Preoperative	37.8 (7.3)	7 (0.9)	38.1 (7.6)	17 (2.3)	−0.2 [−1.0 to 0.5]
HbA1c for non-DM patients		7 (1.1)			
42–47 mmol/mol	49 (6.6)		52 (7.0)		−0.3 [−3.3 to 2.6]
> 47 mmol/mol	8 (1.1)		13 (1.8)		−0.7 [−2.2 to 0.7]

be considered controversial. However, studies have shown that patients developing superficial SSI after primary elective hip or knee arthroplasty have a high risk of progressing into PJI as was found in a recent study where 29% of patients with superficial SSI progressed to PJI [16], and others have shown superficial SSI to increase the risk of PJI 35-fold [17]. Risk of development of superficial SSI has been associated with BMI ≥ 30, HbA1c ≥ 42, and ASA classification ≥ 3 [11,16], which have also been associated with the development of PJI [18]. In our study, PJI occurring within 6 weeks after operation developed in all cases from superficial SSI. Factors influencing superficial SSI to develop into PJI are not only patient dependent but also rely on the virulence of the microorganisms present, which may cause some variation in PJI incidence [19,20].

Effect of optimization in the intervention group waiting for operation

The high awareness and will to influence modifiable risk factors (Table 3, see Appendix) and the general improvement in them while waiting for operation (Table 1) resulted after a rather straightforward optimization pathway, where 93% of the intervention group visited their primary care physician, and those with BMI ≥ 40 and vitamin D deficiency received advice from a hospital-based clinical nutritionist and also consultations from other specialists when deemed necessary. In a recent literature review of preoperative optimization of modifiable risk factors involving 69 studies, only 3 randomized controlled trials and 8 prospective cohort studies were included. Many of the studies mainly observed only 1 modifiable risk factor [1] making comparison with our study somewhat difficult. However, in general, studies on preoperative optimization have shown improvement in SSI [21], PJI [6], total complication rate [21], length of stay [5,22], postoperative emergency ward visits [22], hospi-

Table 2. Continued

Patient characteristics 1 week prior to operation	Intervention group (n = 746)	Missing	Control group (n = 738)	Missing	Difference [CI]
Albumin, g/L ^a	43.4 (2.7)	10 (1.3)	44.2 (2.7)	12 (1.6)	−0.7 [−1.0 to −0.5]
Albumin < 35 g/L	1 (0.1)	10 (1.3)	1 (0.1)	12 (1.6)	0.0 [−0.6 to 0.6]
Lymphocytes < 1.5x10 ⁹ /L	79 (11)	1 (0.1)	129 (18)	2 (0.3)	−6.9 [−10.5 to −3.4]
Vitamin D, nmol/L (SD) ^{a,b}	84.7 (34.5)	5 (0.7)	79.6 (33.9)	16 (2.2)	5.1 [1.6 to 8.7]
Vitamin D < 50 nmol/L ^c	16 (2.1)	20 (2.7)	121 (16)	16 (2.2)	−14.6 [−17.6 to −11.7]
Peri- and postoperative differences					
Blood transfusion	35 (4.7)		19 (2.6)		2.1 [0.2 to 4.1]
Length of stay (days) ^a	1.9 (3.2)		1.7 (1.7)		0.1 [−0.1 to 0.5]
Postoperative medical complications ≤ 6 weeks from operation					
Myocardial infarction			2 (0.3)		
Heart failure	6 (0.8)		3 (0.4)		0.4 [−0.5 to 1.4]
Pneumonia	3 (0.4)		7 (0.9)		−0.5 [−1.6 to 0.4]
Transient ischemic attack	3 (0.4)		7 (0.9)		−0.5 [−1.6 to 0.4]
Pulmonary embolism	5 (0.7)		3 (0.4)		0.3 [−0.6 to 1.2]
Deep vein thrombosis	3 (0.4)		3 (0.4)		0.0 [−0.8 to 0.8]
Renal insufficiency	24 (3.2)		11 (1.5)		1.7 [0.2 to 3.4]
Death	0 (0.0)		0 (0.0)		0.0 [−0.5 to 0.5]

^a Values are mean (SD)

^b Vitamin D results for the intervention group are based on blood tests taken on decision for operation.

^c Results for number of patients with vitamin D < 50 nmol/L 1 week prior to operation in the intervention group are based on repeated blood tests of those 91 patients who had < 50 nmol/L on decision for operation.

Table 5. Comparison of surgical site complications between control and intervention groups within 6 weeks after operation. The difference in proportions between the 2 groups is shown with 95% confidence interval. Values are count (%)

Surgical site complications	Intervention	Missing	Control	Missing	Difference % [CI]
Any surgical site complications	84 (11)	0	116 (16)	3 (0.4)	−4.5 [−8.0 to −1.0]
Superficial SSI	42 (5.6)	0	57 (7.7)	3 (0.4)	−2.1 [−4.7 to 0.4]
Drainage	37 (5.0)	0	58 (7.9)	3 (0.4)	−2.9 [−5.5 to −0.4]
Bleeding	36 (4.8)	0	42 (5.7)	3 (0.4)	−0.9 [−3.2 to 1.4]
Dehiscence	11 (1.5)	0	12 (1.6)	3 (0.4)	−0.2 [−1.5 to 1.2]
Limb hematoma	23 (3.1)	0	13 (1.8)	3 (0.4)	1.3 [−0.3 to 3.0]
Periprosthetic joint infection	11 (1.5)	0	7 (0.9)	3 (0.4)	0.5 [−0.7 to 1.8]

tal readmissions [7], costs [23], and patient engagement [23] to a varying extent. This is in line with our study, where we have shown increased patient engagement and beneficial effects on total complication and superficial SSI rates.

Table 7. Odds ratio (OR) and 95% confidence interval (CI) of superficial surgical site infections (SSI) for patients in the intervention group with preoperative risk factors 1 week prior to operation

Risk factor	OR [CI]	Missing
Preoperative anemia	0.79 [0.18–3.37]	0
HbA1c ≥ 42 mmol/mol	1.13 [0.51–2.51]	7
BMI at operation ≥ 30	1.20 [0.64–2.27]	0
Smoking	2.12 [0.61–7.32]	10
Vitamin D < 50 nmol/L	2.53 [0.55–11.5]	20
Weekly motion ≤ 2	1.52 [0.72–3.20]	163

Comparison of intervention and control group

We did not find any significant association between known modifiable risk factors and superficial SSI in the intervention group. However, in the control group, an association was found with elevated BMI ≥ 30 and HbA1c ≥ 42 mmol/mol [11]. It might be interpreted that by preoperative optimization the associations with these factors in the intervention group were prevented, even though they might be considered at higher risk of complications because of the higher ratio of various comorbidities, also followed by significantly lower odds of developing superficial SSI in the intervention group. This might be explained by the fact that a multidisciplinary approach was used to affect modifiable risk factors, which has been pointed out by others to be necessary for preoperative optimization [24]. Regarding PJI we showed no difference, though our study was not powered to analyze this, but ratios in both groups, i.e., superficial SSI and PJI, are comparable to previous studies [16,25,21].

Limitations

The primary limitation of the study includes a small patient sample in both the intervention and control arms. Additionally, the COVID-19 pandemic affected the execution of the study and slowed down the inclusion of patients, and might have influenced selection of patients into the study, but it is difficult to predict in what manner. The higher ratio of comorbidities in the intervention group may possibly be explained by that the control group was included 1 week prior to operation and no com-

Table 8. Adjusted and crude odds ratio (OR) and 95% confidence interval (CI) of occurrence of superficial surgical site infections in all patients according to preoperative risk factors 1 week prior to operation. 3 observations were deleted due to being missing. Adjustments were made for ASA class II, age, and sex

Risk factor	Adjusted OR [CI]	Crude OR [CI]
Group: intervention	0.64 [0.42–0.97]	0.71 [0.40–1.07]
ASA class II or above	1.83 [1.17–2.82]	
Age	1.02 [0.99–1.04]	
Male sex	1.67 [1.11–2.54]	

mitment by the patient was required. The intervention group was included 6–12 months prior to operation and were offered more contact with the healthcare system but at the same time this also possibly required some commitment from the patient. Therefore, patients with known underlying diseases may have been more willing to participate in the study. Also, a possible higher awareness and fear among patients and physicians in the intervention group of superficial SSI could have increased the number of diagnoses of such infection.

Conclusion

We were able to increase patients' engagement and improve their modifiable risk factors with a structured optimization pathway by cooperation between hospital and primary care. The overall surgical site complication rate was decreased and the odds of developing superficial SSI were reduced in the intervention group.

In perspective, optimizing patients before surgery seems logical but interventions should be studied and their efficacy evaluated.

MS: study initiation and design, data collection, data analysis, manuscript writing. MIS, RDV: data analysis, interpretation of data, manuscript writing. YO, IG: study design, interpretation of data, manuscript writing. ELS: interpretation of data, manuscript writing. SK: study initiation and design, data analysis and interpretation, manuscript writing.

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Appendix

Table 3. Answers to questionnaire by control and intervention groups at preoperative visit 1 week prior to operation. Difference between the 2 groups is shown with 95% confidence interval. Values are count (%)

Answers	Intervention group			Control group			Difference [CI]
	Yes	Not applicable	Missing	Yes	Not applicable	Missing	
<i>During wait for surgery, have you been informed of the following health factors and possible influence of them on the outcome of the operation?</i>							
Weight	613 (82)	35 (4.7)	23 (3.1)	321 (44)	130 (18)	21 (2.8)	38.7 [34.0 to 43.1]
Motion	646 (87)	13 (1.7)	26 (3.5)	381 (52)	112 (15)	18 (2.4)	35.0 [30.5 to 39.2]
Nutrition	591 (79)	19 (2.5)	49 (6.6)	281 (38)	138 (19)	27 (3.7)	41.1 [36.5 to 45.6]
Smoking	355 (48)	276 (37)	48 (6.4)	182 (25)	320 (43)	27 (3.7)	22.9 [18.1 to 27.6]
Anemia	260 (35)	191 (26)	106 (14)	83 (11)	257 (35)	59 (8.0)	23.6 [19.4 to 27.7]
<i>During wait for surgery, have you tried to influence the following health factors?</i>							
Weight	524 (70)	32 (4.3)	38 (5.1)	440 (60)	54 (7.3)	31 (4.2)	10.6 [5.8 to 15.4]
Motion	590 (79)	17 (2.3)	31 (4.2)	500 (68)	45 (6.1)	27 (3.7)	11.3 [6.9 to 15.8]
Use of							
primary care physical activity	83 (11)		482 (65)	42 (5.7)		486 (66)	5.4 [2.6 to 8.3]
physiotherapy	270 (36)		347 (47)	201 (27)		388 (53)	9.0 [4.2 to 13.6]
Motion incidences/week			163 (22)			71 (9.6)	
0	66 (8.8)			114 (15)			−6.6 [−9.9 to −3.3]
1	39 (5.2)			49 (6.6)			−1.4 [−3.9 to 1.0]
2	93 (13)			131 (18)			−5.3 [−8.9 to −1.6]
3	159 (21)			158 (21)			−0.1 [−4.3 to 4.1]
4	115 (15)			93 (13)			2.8 [−0.7 to 6.4]
≥ 5	111 (15)			122 (17)			−1.7 [−5.4 to 2.1]
Motion length, minutes			168 (23)			78 (11)	
0	58 (7.8)			101 (14)			−5.9 [−9.1 to −2.8]
0–20	121 (16)			117 (16)			0.4 [−3.4 to 4.1]
20–40	222 (30)			200 (27)			2.7 [−1.9 to 7.2]
40–60	132 (18)			170 (23)			−5.3 [−9.4 to −1.2]
> 60	45 (6.0)			72 (9.8)			−3.7 [−6.5 to −1.0]
Nutrition	529 (71)	23 (3.1)	52 (7.0)	440 (60)	57 (7.7)	34 (4.6)	11.3 [6.5 to 15.8]
Smoking	142 (19)	422 (57)	92 (12)	102 (14)	450 (61)	66 (8.9)	5.2 [1.4 to 9.0]
Still smoking at time of surgery	28 (3.8)		10 (1.3)	54 (7.3)		11 (1.5)	−3.6 [−6.0 to −1.2]
<i>If previous smoker, when did you quit?</i>			427 (57)			434 (59)	
< 6 weeks	16 (2.1)			6 (0.8)			1.3 [0.1 to 2.7]
6 week to < 6 moths	13 (1.7)			6 (0.8)			0.9 [−0.3 to 2.2]
6 months to < 1 year	15 (2.0)			6 (0.8)			1.2 [0.0 to 2.6]
≥ 1 year	275 (37)			286 (39)			−1.9 [−6.8 to 3.0]
Anemia treated with iron supplement	61 (8.2)	259 (35)	97 (13)	22 (3.0)	323 (44)	90 (12)	5.2 [2.9 to 7.6]
<i>During wait for surgery, have you been in contact with other healthcare providers?</i>							
Primary care	695 (93)			58 (7.9)		102 (14)	85.3 [82.3 to 87.7]
Cardiologist	205 (28)			90 (12)	147 (20)	77 (10)	15.3 [11.3 to 19.2]
Pulmonologist	23 (3.1)	153 (21)	217 (29)	25 (3.4)	180 (24)	90 (12)	−0.3 [−2.2 to 1.5]
Endocrinologist	23 (3.1)	167 (22)	222 (30)	14 (1.9)	206 (28)	90 (12)	1.2 [−0.4 to 2.9]
Nephrologist	21 (2.8)	166 (22)	222 (30)	9 (1.2)	207 (28)	93 (13)	1.6 [0.1 to 3.2]

Table 4. Answers by individuals in intervention group to questionnaire at preoperative visit. Values are count (%)

Answers	Yes	Missing
Appreciation of hospital service		96 (13)
1. Very dissatisfied	100 (13)	
2. Dissatisfied	13 (1.7)	
3. Neutral	53 (7.1)	
4. Satisfied	219 (29)	
5. Very satisfied	265 (36)	
Appreciation of primary care service		355 (48)
1. Very dissatisfied	30 (4.0)	
2. Dissatisfied	10 (1.3)	
3. Neutral	98 (13)	
4. Satisfied	144 (19)	
5. Very satisfied	109 (15)	
Noticed hospital and primary health care cooperation		224 (30)
1. Did not notice	146 (20)	
2. Vaguely noticed	78 (11)	
3. Noticed	183 (25)	
4. Aware	82 (11)	
5. Well aware	33 (4.4)	

Table 6. Positive bacterial cultures in superficial surgical site infections (SSI) and periprosthetic joint infections (PJI). Values are count (%)

Factor	Intervention group (n = 746)	Control group (n = 738)
Superficial SSI	42 (5.6)	57 (7.7)
Cultures taken	20/42 (48)	28/57 (49)
Cultures positive	15/20 (75)	18/28 (64)
Bacteria considered the main cause of infection		
Staphylococci		
<i>S. aureus</i>	9	10
<i>S. epidermidis</i>	4	3
Coagulase negative s.	1	3
<i>S. caprae</i>		1
<i>Pseudomonas</i>		1
<i>Enterococcus faecalis</i>	1	
Additional bacteria cultured		
<i>Enterococcus faecalis</i>		1
Corynebacter		1
<i>Proteus mirabilis</i>		1
<i>Escherisia coli</i>		1
<i>Streptococcus agalactiae</i>		1
Enterobacter	1	
No. of patients with multibacterial infection	1	3
PJI	11 (1.5)	7 (0.9)
Cultures taken	11/11	7/7
Cultures positive	11/11	7/7
Bacteria considered the main cause of infection		
Staphylococci		
<i>S. aureus</i>	6	3
<i>S. epidermidis</i>	3	1
<i>S. caprae</i>		1
<i>Streptococcus agalactiae</i>		1
<i>Proteus mirabilis</i>		1
Acinetobacter B.	1	
<i>Enterococcus fecalis</i>	1	
Additional bacteria cultured		
<i>S. lugudensis</i>		1
<i>Corynebacterium tuberculosteanicum</i>	1	
<i>Dermabacter hominis</i>		1
<i>Acinetobacter pittii</i>		1
<i>S. epidermidis</i>	2	1
<i>Micrococcus luteus</i>	1	
Corynebacterium	1	
Brevibacterium	1	
<i>Aerococcus viridans</i>	1	
Dermabacter	1	
No. of patients with multibacterial infection	3	2

Paper III

Prospective long-term follow-up of surgical complications and general health after preoperative optimization for primary arthroplasty

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Prospective long-term follow-up of surgical complications and general health after preoperative optimization for primary arthroplasty

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Abstract

Background and purpose

Preoperative optimization programs aim to reduce complications after total joint arthroplasty (TJA), yet long-term effects on superficial surgical site infections (SSI), periprosthetic joint infections (PJI), and overall health remain unclear. This study evaluated the long-term impact of a structured preoperative optimization pathway in cooperation of hospital and primary care on infection outcomes and general health following elective primary lower extremity TJA.

Patients and methods

In this prospective case-control study, 1,484 patients undergoing TJA between 2018 and 2022 were followed postoperatively. The intervention group (n=746) underwent a multi-factorial optimization process 6–12 months preoperatively, while the control group (n=738) received conventional preparation. Outcomes included incidence of superficial SSI and PJI, postoperative health diagnoses/events, and mortality. Fine-Gray competing risk models and negative binomial regression were used for statistical analyses.

Results

Superficial SSI occurred in 5.9% of the intervention group vs. 7.9% in the control (HR 0.67; 95%CI 0.45–1.01). PJI occurred in 2.0% vs. 1.1%, respectively (HR 1.80; 95% CI 0.76–4.30). Most PJIs (80–88%) followed superficial SSI. Progression from superficial SSI to PJI was higher in the intervention group (27.3% vs. 12.1%). No significant differences were found in new postoperative health diagnoses, events, or mortality.

Conclusion

Although short-term benefits of preoperative optimization have been previously reported from this project, this study found no statistically significant long-term reductions in superficial SSI, PJI, or general health. Confounding factors, including Covid-19 related disruptions and organizational changes, may have influenced outcomes. Continued prospective evaluation of optimization strategies is warranted.

Introduction

Lower extremity total joint arthroplasty (TJA) reduces pain and improves quality of life of individuals with end-stage osteoarthritis. The incidence of TJA operations continues to rise, with favorable outcomes in majority of cases, and prosthesis 10-years survival rate over 95% (1). However, complications may follow TJA with superficial surgical site infection (SSI) estimated to occur in 1-10% of cases, with high risk of progression into periprosthetic joint infection (PJI) (2). This complication is devastating and costly for patients and society, requiring repeated surgeries, longstanding antibiotic treatment and is associated with increased morbidity and mortality (1). The incidence of PJI after TJA is between 0.5 - 2,8%, varying between countries (1,3)

Consequently, it has been pointed out that prevention of infections is more important than diagnoses and treatment (4) leading to growing interest in preoperative optimization programs to improve modifiable risk factors before TJA to reduce complications and costs, and improve health outcomes after surgery (5).

There is a wide variety in how preoperative optimization has been approached. Organization may be within hospital, primary care, special clinics or a combination (6-8). The choice and number of health factors addressed differs and varies between medical, psychological and physical conditions of patients as well as socioeconomic status (5,9).

However, little has been published about the efficacy of such programs (10,11) and their possible long-term effect on general health (12). We have previously reported an optimization pathway, developed in collaboration of hospital and primary care, that increased patient engagement and improved modifiable risk factors preoperatively, leading to fewer surgical site complications and significantly reduced odds of developing superficial SSI within six weeks after surgery (13).

The aim of this study was to prospectively estimate long-term infectious surgical outcomes and effect on general health for patients undergoing preoperative optimization compared with conventional preparation.

Methods

This was a prospective case control study conducted at a single institution. The control (14) and the intervention groups and their comparisons up to 6 weeks postoperatively have been described previously (13) with methods, parameters and definitions used.

Patients in the control group were already registered on the TJA waiting list and enrolled between August 2018 and September 2020 during a preoperative clinic visit one week before surgery. They had received standard preoperative advice on weight, smoking, and lifestyle from their orthopedic surgeon at decision of operation without follow-up.

Patients in the intervention group were enrolled between January 2019 and January 2021 at the outpatient orthopedic clinic after referral from primary care 6 – 12 months before surgery. Baseline blood tests were taken, and BMI recorded, with follow-up by their primary care physician within 3 weeks, focusing on obesity, glycemic control, anemia, nutritional status, smoking cessation, and exercise. Patients with BMI ≥ 40 were referred to a clinical nutritionist, and those with vitamin D < 50 nmol/L were advised to take supplements. Malnutrition risk was assessed.

One week before surgery both groups had blood tests and BMI recorded and completed a questionnaire regarding the preoperative process.

The control group had surgery from August 2018 to September 2020 and the intervention group from March 2019 to December 2022. Both were followed postoperatively until May 2025.

Data registration included surgery details, demographics, anesthesia type, ASA class, laboratory variables, blood transfusions, length of stay, postoperative complications and mortality. Superficial SSI and PJI were diagnosed according to validated definitions (15,16). Details on joint-related complications postoperatively were recorded for those who required further surgery.

Patient records from both primary care and hospital were reviewed to identify new postoperative health issues defined as diagnosis of hypertension, arrhythmia, ischemic heart disease, heart failure, aortic stenosis, diabetes, obstructive lung disease, worsening of kidney function, prescription of GLP-1 agonists, increase in BMI and cancer. Furthermore, the occurrence of new health related events defined as myocardial infarction, cardiac arrest, pneumonia, deep vein thrombosis, pulmonary embolism and transient ischemic attack were also recorded.

Information from the hospital electronic health records additionally included visits to emergency department, admission to hospital and admission to ICU that occurred postoperatively.

Statistical analysis

Data are presented as frequencies and percentages for categorical variables and median (interquartile range [IQR]) for numerical variables unless otherwise specified. Statistical significance was set at $\alpha = 0.05$.

Fine-Gray sub-distribution hazard models were used to analyze superficial SSI and PJI, treating death as a competing risk and adjusting for sex, age, and ASA score.

Cumulative incidence functions were estimated using Aalen-Johansen method, with Gray's test comparing incidence curves across groups, accounting for death as a competing risk.

For count outcomes involving cumulative postoperative new illness diagnoses and health events, negative binomial regression was used to calculate incidence rate ratios with offset terms for variable follow-up duration. Both crude and adjusted models were fitted, controlling for age, sex, and ASA score.

Univariate logistic regression was used to evaluate associations between modifiable risk factors (anemia, HbA1c ≥ 42 mmol/mol, BMI ≥ 30 , smoking, vitamin D insufficiency, lack of exercise) and superficial SSI, stratified by treatment group.

Kaplan-Meier survival analysis was performed for mortality outcomes, with log-rank tests for group comparisons.

Missing data was negligible for primary clinical variables. All analyses were performed using R version 4.5.0 (R Foundation for Statistical Computing, Vienna, Austria).

Ethics, registration, funding, and disclosures

The study was approved by the Science Committee of Primary Care in the Capital Area and the Icelandic National Bioethics Committee (VSN-18098) and registered on ClinicalTrials.gov (NCT05399186). Funding was provided by the Landspítali Research Fund and the Sigríður Lárusdóttir Research Fund. The authors declare no conflict of interest.

Results

The control group consisted of 738 of 744 consenting patients included one week before operation between August 2018 – September 2020 (69% of eligible patients). The intervention arm consisted of 746 of 1.010 consenting patients included at median 307 days ([206 – 447], range 18-1322) before operation between January 2019 – January 2021 (43% of eligible patients), with 259 exclusions due to declined surgery when offered. The control group had surgery between August 2018 – September 2020 and the intervention group between Mars 2019 – December 2022, or 5% versus 77% during the Covid-19 pandemic respectively.

Long term follow-up after TJA

As the control group had their operations earlier in the observational period there were a higher number of patients in the control group with follow up over 3 years (table 1S). A cut was made at one year for analysis of superficial SSI and three years for other parameters.

Flow chart of long-term outcomes after operation for both groups regarding superficial SSI, Debridement, Antibiotics and Implant Retention (DAIR) operations, Two Stage operations and revision arthroplasties are shown in Fig 1S. Revisions arthroplasties were more commonly performed in the intervention group, or 3.5% versus 1.9% (Fig 1S).

Time factors

The median time from operation to diagnosis of the 44 superficial SSI in the intervention group was 21 days ([15 – 33], range 1-60), and of the 58 in the control group 18 days ([14 – 29], range 2-132).

The median time from operation to diagnosis of the 15 PJI in the intervention group was 31 days ([26 – 52], range 15-1056), and of the 8 in the control group 26 days ([22 – 36], range 17-512).

For those patients with superficial SSI that developed PJI the median time between the two diagnosis was for the 12 cases in the intervention group 6 days ([2 – 8], range 2-8), and for the 7 in the control group 4 days ([4 – 12], range 1-15).

Hazard ratio for superficial SSI and PJI

At one year the occurrence of superficial SSI was less common in the intervention group or 5.9% versus 7.9% in the control group. A Fine-Gray risk model adjusted for sex, age and ASA score showed a lower hazard ratio of superficial SSI in the intervention group, albeit the difference was not significant, HR 0.67; 95%CI 0.45 – 1.01.

A crude estimate of the group effect on cumulative incidence of superficial SSI over one year post-operatively showed no significant difference between intervention and control groups (Gray's test $p = 0.132$). When stratified by ASA score, cumulative incidence was highest in the control group with ASA 3-4, with significant differences detected among the four curves (Gray's test $p = 0.002$). Similarly, when stratified by BMI categories, cumulative incidence was highest in the control group with BMI ≥ 30 , with significant differences among the four curves (Gray's test $p = 0.041$) (Fig. 3).

At 3 years PJI was more common in the intervention group or 2.0% versus 1.1%. A Fine-Gray risk model adjusted for sex, age and ASA score showed a higher hazard ratio of PJI in the intervention group though without significant difference 1.80; 95%CI 0.76 – 4.30.

A crude estimate of the group effect on cumulative incidence of PJI over three years post-operatively showed no significant difference between intervention and control groups (Gray's test $p = 0.142$).

When stratified by ASA score, cumulative incidence was highest in the intervention group with ASA 3-4, with no significant differences detected among the four curves (Gray's test $p = 0.174$). When stratified by BMI categories, cumulative incidence was highest in the intervention group with BMI ≥ 30 , with significant differences among the four curves (Gray's test $p = 0.009$) (Fig. 4).

Progression from superficial SSI to PJI

Superficial SSI preceded PJI in 80% (12/15) of cases in the intervention group and 88% (7/8) in the control group.

In the intervention group 12 of 44 patients with superficial SSI progressed to PJI (27.3%) but in the control group 7 of 58 (12.1%).

The proportion of superficial SSI progressing to PJI was higher in both ASA 1-2 and ASA 3-4 categories in the intervention group compared to the control group. The highest progression proportion was, however, in the intervention group among patients with BMI ≥ 30 , or 37% (Table 2).

Association between preoperative risk factors and development of superficial SSI

A univariable logistic regression analysis showed no association between superficial SSI at 1 year and the presence of known preoperative risk factors in the intervention group, but an association was found with elevated BMI ≥ 30 and HbA1c ≥ 42 mmol/mol in the control group (table 3).

Effect on postoperative general health

When looking at health related diagnoses and events preoperatively their total occurrence was higher in the intervention group than in the control group, reflected in higher ASA score in the intervention group (13). This pattern became the opposite postoperatively both regarding new diagnosis and events (figure 5). A negative binomial regression analysis calculating incidence rate ratios (IRR), accounting for variable follow-up time and adjusting for age, sex, and ASA score, showed no significant difference for IRR for in health-related diagnosis 0.79; 95%CI 0.61 – 0.1.02 nor in health-related events 0.94; 95%CI 0.59 – 1.49.

When analyzing the cumulative incidence of first health related diagnosis and event after operation there was no significant difference between the curves regarding first health related diagnosis with lower incidence in the intervention group, or 16.6% versus 20.5%. Neither was there a significant difference regarding new health-related events, or 5.1% versus 5.3% (figure 7).

There was a similar cumulative incidence between the intervention and control groups when comparing first visits after surgery to emergency department (46.0% versus 44.6%), admission to hospital (39.4% versus 41.6%) and intensive care (4.7% versus 4.5%) without significant difference between curves (figure 8).

Effect on mortality

There was no significant difference in survival curves between the treatment groups (log-rank test $p = 0.553$), with 3-year survival at 98.1% in the intervention group versus 97.6% in the control group. When stratified by ASA score, there were significant differences among the four survival curves (log-rank test $p < 0.001$), while no significant differences were detected among curves when stratified by BMI categories (log-rank test $p = 0.909$) (Figure 9).

Types of bacteria

Positive cultures showed common bacteria known to cause PJI. Staphylococci were the cause of infection in the one case of PJI that occurred in the control group more than six weeks after operation but in 2 of the 4 that occurred in the intervention group while streptococci were the cause in the other 2 (table 4S).

Discussion

This study shows that an optimization effort of modifiable risk factors did not decrease the incidence of superficial SSI significantly when registered one year after primary TJA. At three years there was neither a difference in the occurrence of PJI nor a noticeable effect on general health of patients. However, substantial changes in organization and conditions during the study may have affected results.

Short term outcomes

The outcomes at 6 weeks have been previously reported showing that the optimization effort increased patient engagement and improved modifiable risk factors before operation, leading to fewer surgical site complications and significantly reduced risk of superficial SSI but did not affect occurrence of PJI (13).

Long term outcomes

Superficial SSI

We chose superficial SSI as the primary outcome to increase the likelihood of detecting significant differences given the available sample size. This may be debated but is supported by evidence that superficial SSI often precedes PJI (2) as was the case in vast majority in our study. The time frame for registering superficial SSI varies, from 30 days (17) to 6 months (18). We used a one-year cutoff, with the last case diagnosed 132 days postoperatively. However, most cases (95% in the intervention group, 98% in the control group) were diagnosed within 6 weeks.

Reported superficial SSI rates after TJA range from 1–10% (2), aligning with our findings: 5.9% in the intervention group and 7.9% in the control group, with a significant difference at 6 weeks (13), and overall similar rates at one year.

When looking at cumulative incidence of superficial SSI it appeared more associated with ASA score than BMI.

At one year, of the observed risk factors, elevated BMI and HbA1c were associated with superficial SSI only in the control group, the same pattern as at six weeks (13), possibly suggesting that optimization may have mitigated risk in the intervention group despite higher comorbidities.

PJI

At three years, PJI had occurred in 2.0% of cases in the intervention group and 1.1% in the control group, both within reported ranges (1,5). Most PJIs (80% in the intervention group, 87% in the control) developed from superficial SSI, typically within a week of the superficial SSI diagnoses, indicating infection burden was concentrated in the first 6 weeks postoperatively.

The progression ratio from superficial SSI to PJI was higher in the intervention group (27.3%) than in the control group (12.0%), though similar to rates in recent literature (29%) (2). Factors influencing this progression remain unclear, but it likely depends on both patient characteristics and

microorganism virulence (2,19). The intervention group had a higher ratio of patients with BMI ≥ 30 and ASA score 3-4 than the control group possibly affecting this.

Progression was highest among patients in the intervention group with BMI ≥ 30 (37%) and when looking at cumulative incidence BMI appeared more related to PJI risk than ASA score, though a recent study suggests ASA may be a stronger predictor (20).

Effect on postoperative general health

Preoperative optimization has been shown to reduce infection rates (7,21), complications (21), hospital stay (6,22), readmissions (8), costs (23), and improve patient engagement (23).

Our findings align somewhat, showing increased patient engagement and reduced short-term surgical complications and superficial SSI (13), though we observed no long-term effect on general health.

The intervention group initially had more patients with ASA scores of 3–4, reflected in a higher rate of preoperative health-related diagnoses and events (13). Postoperatively, this reversed, with more new diagnoses and events in the control group, possibly due to earlier detection in the intervention group from greater preoperative healthcare contact, though differences were not significant.

Postoperative cumulative rates of new diagnoses, and events and first visits to emergency department, admission to hospital and ICU were similar between groups.

Mortality rates were also similar, but significantly higher in ASA 3–4 than ASA 1–2 groups but no such pattern was seen between BMI groups in line with a recent study (24).

Types of bacteria

The most common causative organisms for PJI were Gram-positive species, with Staphylococci being the most common which is similar as in other studies (19).

Limitations

The groups: The study groups were small and not fully comparable. The intervention group had more patients with comorbidities, reflected by a higher proportion with ASA scores of 3–4 (32% vs. 23%) and slightly more with BMI ≥ 30 (55% vs. 52%) despite optimization (13). Heightened awareness and concern about superficial SSIs in the intervention group may also have led to more frequent diagnoses.

Patient selection: In 2021, due to long waiting times, Icelandic health officials arranged for TJA procedures at rural hospitals and a private clinic began offering TJA as well. Patients waiting over three months could also opt for surgery abroad under EEA/EU regulations. These factors likely contributed to a high number of patients declining surgery in the intervention group and a higher ASA score among those who participated.

Covid-19: The Covid-19 pandemic caused disruption and delay of the study. Only 5% of the control group had surgery during it compared to 77% of the intervention group. During the pandemic staffing, prioritization of surgical procedures and pre- and postoperative practices were affected. Social restrictions may have influenced the quality of follow-up.

Reports on Covid-19's effect on outcomes after TJA vary. Some report decline in SSI (25), others no change (26), while some found increase in SSI (27), especially in newly operated patients contracting Covid-19 (28). It is therefore difficult to predict the effect of Covid-19 pandemic on our study cohort.

Bacterial factors: Increased susceptibility to infections in the initial post Covid-19 years have been reported (29,30). This may have affected the groups differently based on surgery timing, possibly influencing the progression from superficial SSI to PJI.

Strengths

The study's main strength is its prospective nature, detailed data collection, thorough follow-up, and minimal missing clinical data.

Conclusions

A preoperative optimization effort of modifiable risk factors did not significantly reduce superficial SSI at one year or PJI at three years, nor did it have effect on general health outcomes. Changes during the study, particularly transfer of TJA procedures to other facilities and the Covid-19 pandemic may have influenced results by affecting patient selection and patient care practices.

This study reveals the importance of performing long term prospective studies on preoperative optimization as well as estimating the effect of organizational and practice changes on patient care.

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Tables 1-4 (table 1S and 4S are meant for supplement)

Table 1S. Number of patients followed up per year after surgery.

	Number of patients followed per year after operation (%)				
	1 yr	2 yr	3 yr	4 yr	5 yr
Intervention group: no 746	741 (99)	692 (93)	549 (74)	178 (24)	1 (0,1)
Control group: no 738	735 (99)	731 (99)	723 (98)	684 (93)	262 (36)

Table 2. Conversion rate of superficial SSI (SSSI) to PJI according to ASA and BMI score. Results are shown as count (%).

	Intervention group 746					Control group 738				
	No (%)	SSSI (6%)	PJI total (2.0%)	PJI without preceding SSSI	PJI generated from SSSI (progression ratio%)	No (%)	SSSI (8%)	PJI total (1.1%)	PJI without preceding SSSI	PJI generating from SSSI (progression ratio%)
ASA 1-2	510 (68)	23 (3)	8 (1.1)	2	6 (27.3)	572 (78)	37 (5)	5 (0.7)	1	4 (10.8)
ASA 3-4	236 (32)	21 (3)	7 (0.9)	1	6 (30.4)	166 (22)	21 (3)	3 (0.4)		3 (14.3)
BMI <30	334 (45)	17 (2)	2 (0.3)		2 (11.8)	354 (48)	20 (3)	2 (0.3)		2 (10.0)
BMI ≥30	412 (55)	27 (4)	13 (1.7)	3	10 (37.0)	384 (52)	38 (5)	6 (0.8)	1	5 (13.2)

Table 3. Odds Ratios for Risk Factors Associated with Superficial Surgical Site Infection (SSI). (OR = Odds Ratio; CI = Confidence Interval. Missing data displayed as count/total (percentage)).

	Intervention group		Control group	
	OR (95% CI)	Missing data	OR (95% CI)	Missing data
BMI at operation ≥ 30	1.31 (0.70-2.44)	0/746 (0.0%)	1.83 (1.04-3.21)	1/738 (0.1%)
HbA1c ≥ 42 mmol/mol	1.06 (0.48-2.35)	7/746 (0.9%)	2.09 (1.11-3.91)	17/738 (2.3%)
Preoperative anemia	0.75 (0.18-3.20)	0/746 (0.0%)	0.89 (0.31-2.56)	2/738 (0.3%)
Vitamin D < 50 nmol/L	1.14 (0.47-2.77)	5/746 (0.7%)	0.93 (0.44-1.94)	16/738 (2.2%)
Smoking	2.00 (0.58-6.92)	10/746 (1.3%)	1.19 (0.46-3.12)	11/738 (1.5%)
Weekly exercise ≤ 2	0.61 (0.29-1.26)	163/746 (21.8%)	0.92 (0.52-1.64)	71/738 (9.6%)

Table 4S. Positive bacterial cultures ≤6 weeks and >6 weeks up to 1 year in superficial SSI and up to 3 years in PJI after primary total joint arthroplasty. Values are count (%)

	Intervention group (n = 746)		Control group (n = 738)	
	≤6w	>6w	≤6w	>6w
Superficial SSI	42 (5.6)	2 (0.27)	57 (7.7)	1 (0.14)
Cultures taken	20	1	28	1
Cultures positive	15	1	18	1
Bacteria considered the main cause of infection				
Staphylococci				
<i>S. aureus</i>	9		10	1
<i>S. epidermidis</i>	4		3	
<i>Coagulase negative s.</i>	1		3	
<i>S. caprae</i>			1	
Streptococci				
<i>Str. dysgalactiae</i>		1		
<i>Pseudomonas</i>			1	
<i>Enterococcus faecalis</i>	1			
Additional bacteria that were cultured				
<i>Enterococcus faecalis</i>			1	
<i>Corynebacter</i>			1	
<i>Proteus Mirabilis</i>			1	
<i>Escherisia coli</i>			1	
<i>Streptococcus agalactiae</i>			1	
<i>Enterobacter</i>	1			
No. of patients with multibacterial infection	1		3	
PJI	11 (1.5)	4 (0.54)	7 (0.95)	1 (0.14)
Cultures taken	11	4	7	1
Cultures positive	11	4	7	1
Bacteria considered the main cause of infection				
Staphylococci				
<i>S. aureus</i>	6	1	3	
<i>S. epidermidis</i>	3	1	1	1
<i>S. caprae</i>			1	
Streptococci				
<i>Str. dysgalactiae</i>	0	1		
<i>Str. pneumoniae</i>	0	1		
<i>Str. agalactiae</i>			1	
<i>Proteus Mirabilis</i>			1	
<i>Acinetobacter B.</i>	1			
<i>Enterococcus Fecalis</i>	1			
Additional bacteria cultured				
Staphylococci				
<i>S. captis</i>		1		
<i>S. Lugudensis</i>			1	
<i>S. epidermidis</i>	2		1	
<i>Corynebacterium tuberculos.</i>	1			
<i>Dermabacter hominis</i>			1	
<i>Acinetobacter pittii</i>			1	
<i>Micrococcus Luteus</i>	1			
<i>Corynebacterium</i>	1			
<i>Brevibacterium</i>	1			
<i>Aerococcus Viridans</i>	1			
<i>Dermabacter</i>	1			
No. of patients with multibacterial infection	3	1	2	

Figures (Figur 1S is meant for supplement)

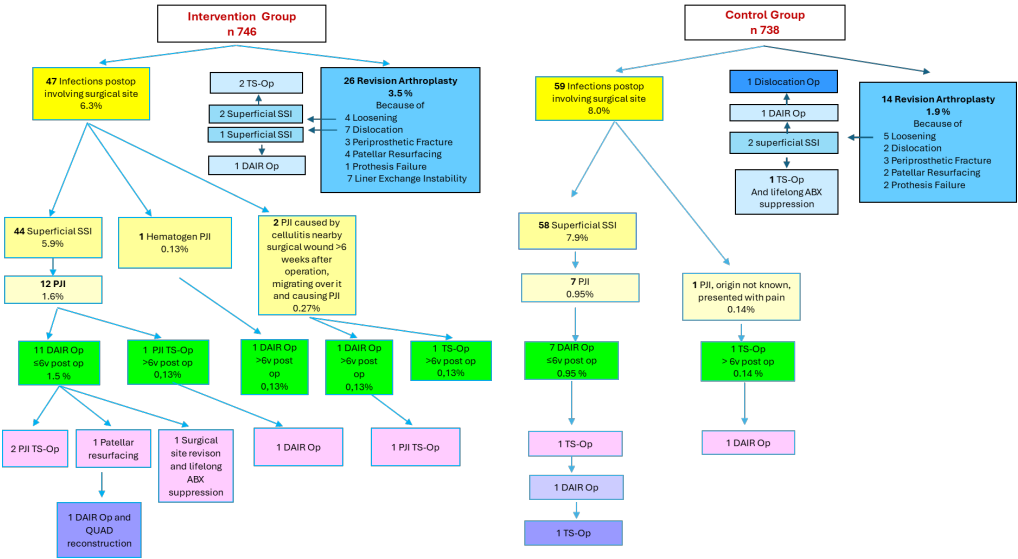
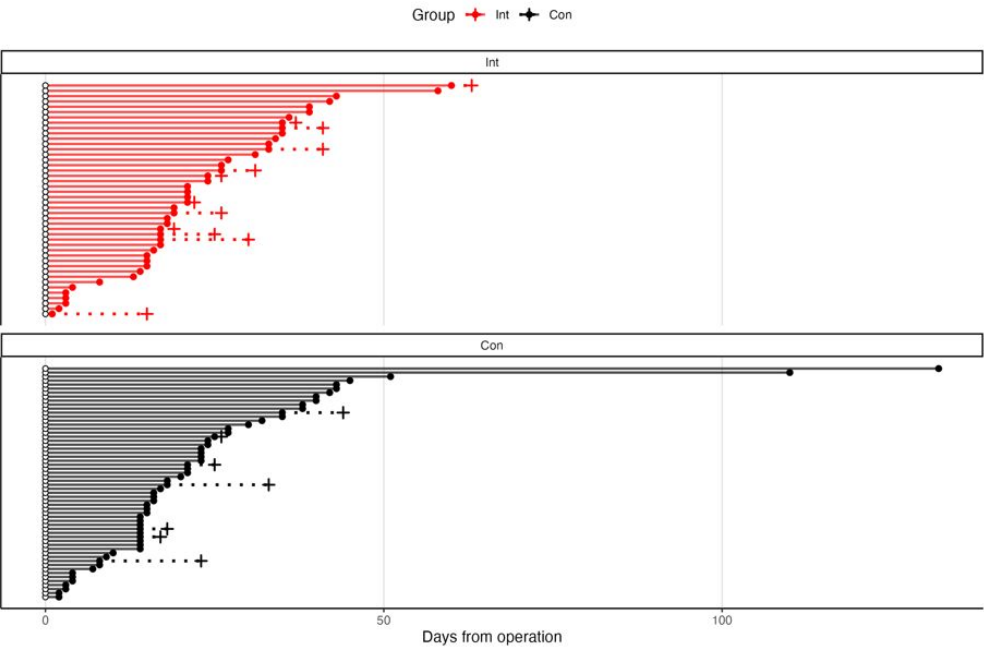


Fig 1S. Postoperative infectious complications and revisions arthroplasties after primary joint arthroplasty in intervention and control groups (DAIR Op: debridement, antibiotics and implant retention, TS-Op: Two Stage operation).

a)

Timeline of SSI patients (with or without subsequent PJI)
Solid lines: time to SSI (●); dotted lines: time to subsequent PJI (+)



b)

Timeline of PJI-only patients (without SSI)
Dotted lines: time to PJI (+)

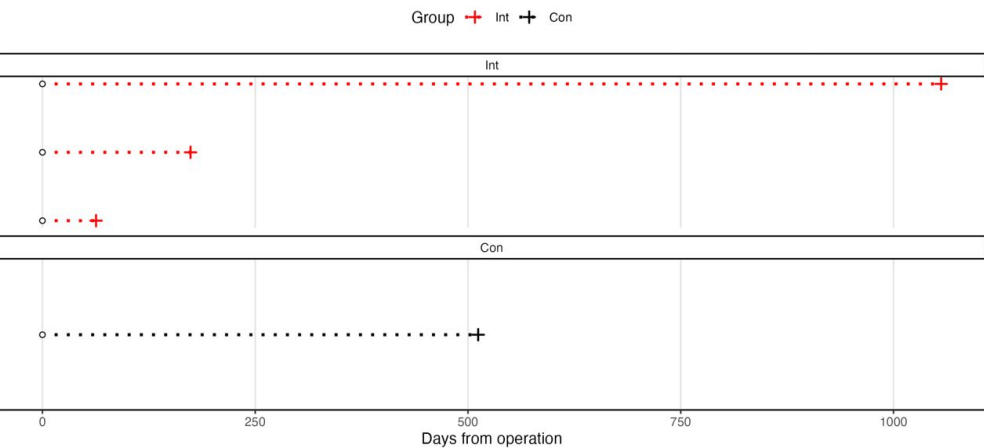


Figure 2. a) Time from surgery to diagnosis of superficial SSI after primary TJA (whole line) and time to diagnosis of PJI after preceding superficial SSI (dotted line). b) Time from surgery to diagnosis of PJI after TJA without preceding superficial SSI.

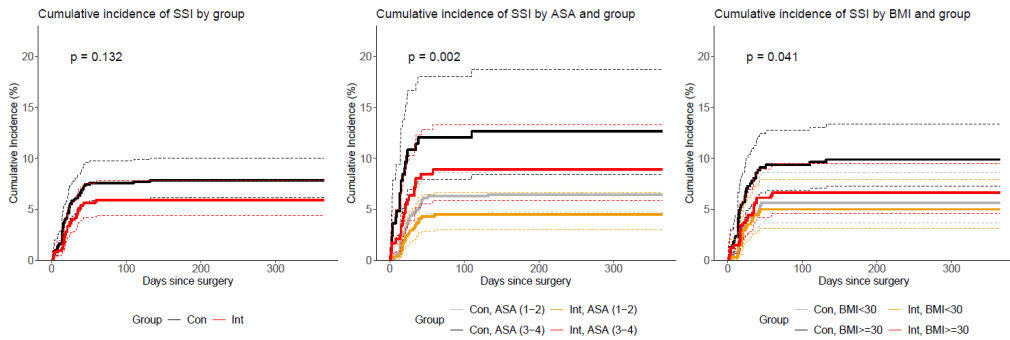


Fig 3. Cumulative incidence of superficial SSI by group, ASA and BMI categories at 1 year follow up

30, with significant differences among the four curves (Gray's test $p = 0.009$) (Fig. 4).

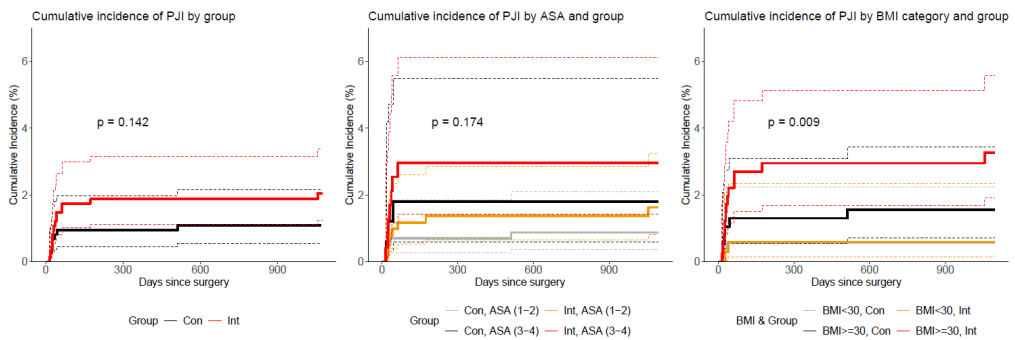


Fig 4. Cumulative incidence of PJI by group and ASA and BMI scores at three years follow up time.

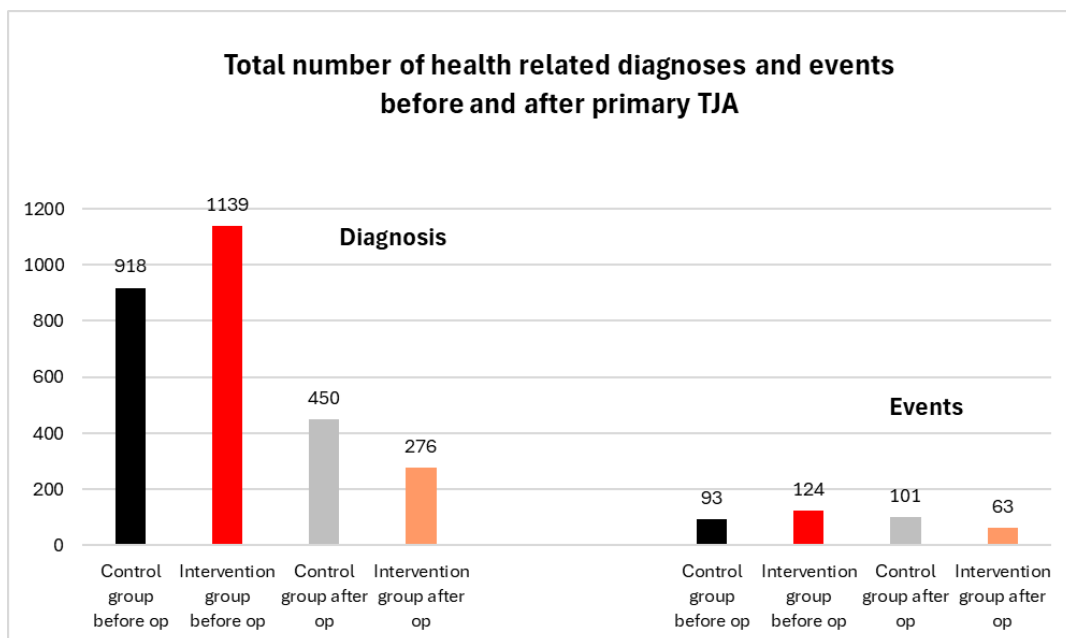


Figure 6. All health-related diagnosis and events before and after operation

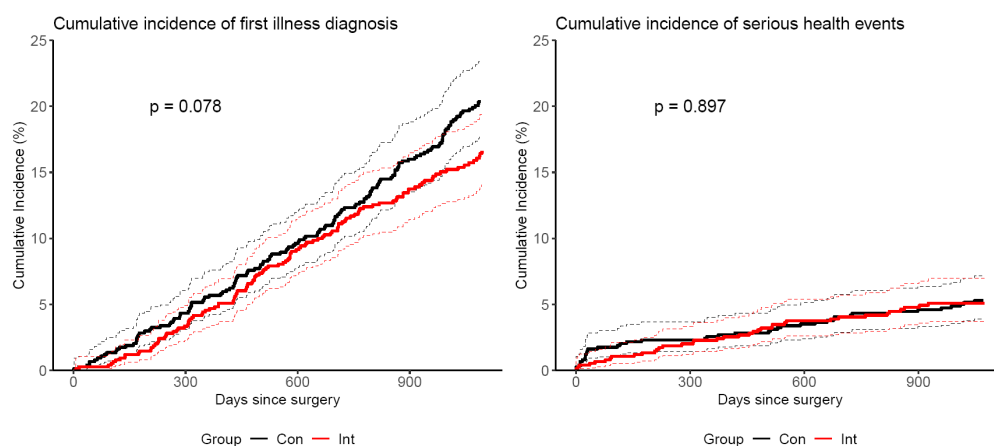


Figure 7. Cumulative incidence of first health related diagnosis and events postoperatively

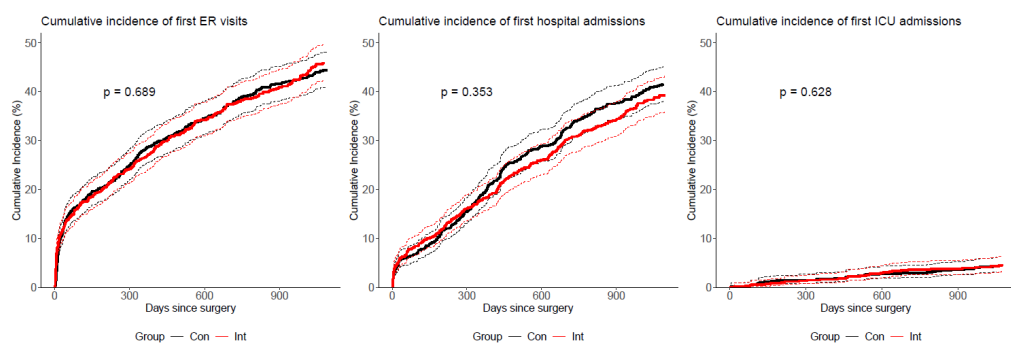


Figure 8. Cumulative incidence first postoperative visits to emergency department and admission to hospital and ICU

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	4
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	4,5
Study size	10	Explain how the study size was arrived at	4

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4,5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	4,5
		(b) Describe any methods used to examine subgroups and interactions	NA
		(c) Explain how missing data were addressed	5
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	4
		(e) Describe any sensitivity analyses	NA

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6 Fig S1
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	Fig S1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6 Table 4
		(b) Indicate number of participants with missing data for each variable of interest	Table 4
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	6, Table 1S
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	NA
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	6-12 Tables 1S, 2, 6S

			Fig 1S,2-8
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	NA
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-12
		(b) Report category boundaries when continuous variables were categorized	6 -12
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14 -16
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	5

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

Appendix I

This screening sheet should be used to assess the need for nutritional therapy among adult patients.

*Answer the following questions and give score accordingly.
 If a patient scores 6 or more points, a referral should be sent to the Department of Clinical Nutrition.*

PATIENT'S I.D.

QUESTION	ANSWER	ASSESSMENT	POINTS
----------	--------	------------	--------

1. Height: _____ m Weight: _____ kg	BMI: Kg/m ² _____	>20 0 point 18-20: 2 points <18: 4 points	_____
2. Recent unintentional weight loss? If yes, how much? _____ kg In what time period? _____ months	☐ Yes ☐ No Weight loss % _____	Unintentional weight loss: >5% past month or > 10% previous 6 mo. 4 points 5-10% " 1-6 mo. 2 points Other 0 point	_____
3. Age over 65 years?	☐ Yes ☐ No	Questions 3 to 8: Yes: 1 point No: 0 point	_____
4. Avoids 2 or 3 of following: Meat, fish, dairy products?	☐ Yes ☐ No		_____
5. Problems last weeks or months? A. Vomiting lasting more than 3 days ? B. Daily diarrhoea (more than 3 liquid stools per day)? C. Continuous loss of appetite or nausea? D. Difficulty in chewing or swallowing?	☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No		_____ _____ _____ _____
6. Hospitalized for 5 or more days during previous 2 months?	☐ Yes ☐ No		_____
7. Major surgery in the past month? If yes, list type _____	☐ Yes ☐ No		_____ _____
8. Takes 8 or more medicines daily?	☐ Yes ☐ No		_____
9. Diseases			
1 point	3 points	6 points	
☐ Celiac disease	☐ Alcoholism	☐ Major burn, > 15 %	
☐ Abdominal pain	☐ Anorexia nervosa	☐ Malnutrition	
☐ Esophageal stricture	☐ Cancer	☐ Multiple trauma	
☐ Intestinal obstruction	☐ Cirrhosis		
☐ Gangrene	☐ Crohn's disease		
☐ Hyperemesis gravidarum	☐ Ulcerative colitis		
☐ Anemia	☐ Gastrointestinal hemorrhage		
☐ Benign tumor	☐ Hepatic disease		
☐ Pyrexia of unknown origin	☐ Cystic fibrosis		
☐ Decubitus ulcer	☐ Malabsorption		
☐ Septicemia	☐ Cell immune deficiency		
☐ Diabetes out of control	☐ Renal disease		
☐ Multiple sclerosis	☐ Multiple fractures		
☐ Congestive heart failure	☐ Motor neurone disease (MND)		
☐ Cerebral palsy	☐ Burn, 10-15%		

Completed by _____ Date _____

signature

Sum of
points _____

